

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

SERGEANTS BENEVOLENT
ASSOCIATION HEALTH AND
WELFARE FUND on behalf of itself
and all others similarly situated

Plaintiff,

v.

ELI LILLY AND COMPANY

Defendant

CLASS ACTION COMPLAINT
AND DEMAND FOR JURY
TRIAL

U.S. DISTRICT COURT E.D.N.Y.
BROOKLYN OFFICE

★ NOV 21 2006 ★

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WEINSTEIN, J.

MANN, M.J.

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I. INTRODUCTION

1. This is a proposed national class action on behalf of third party payors (self-insured employers, Taft-Hartley funds, non-profit and for-profit health insurers, all of whom bear the ultimate risk for prescription drug expense) against Eli Lilly & Company ("Lilly" or "Defendant") seeking damages and other monetary relief by reason of Lilly's wrongful and illegal marketing, sales and promotional activities for the atypical antipsychotic Zyprexa.

2. From the 1996 product launch of Zyprexa to the present, Lilly engaged in widespread fraudulent statements and conduct, and pervasive false and misleading marketing, advertising and promotion of Zyprexa. Lilly deceived physicians, consumers, third party payors, and others regarding the comparative efficacy of Zyprexa to other traditional and atypical antipsychotics. Lilly failed to warn – and affirmatively misled – physicians, consumers, third

party payors, and others in the medical community regarding Zyprexa's association with diabetes, diabetes-related conditions and other adverse effects. And even though Zyprexa is an antipsychotic drug and thereby limited in its FDA-approved indications, Lilly actively marketed and promoted Zyprexa for unapproved uses in several populations where the efficacy and safety of the drug had yet to be established -- marketing Zyprexa for the treatment of various conditions or symptoms in children, marketing Zyprexa for treatment in the elderly for dementia, and marketing Zyprexa for treatment of "soccer moms" who experience depressive or other physiological conditions.

3. Lilly's unlawful campaign of marketing, advertising and promoting Zyprexa was highly effective. Although less than one percent of the United States population suffers from diagnosed schizophrenia, and while the drug therapeutic category of antipsychotics has multiple traditional and atypical antipsychotics, within a few short years Zyprexa's annual United States sales exceeded \$3 billion, becoming the leading atypical antipsychotic on the market and Lilly's number one prescription product.

4. Lilly could not accomplish the deceptions regarding comparative efficacy, lack of adverse side effects and demand for non-indicated Zyprexa usage on its own. Not only did Lilly itself make false statements and endorse half-truths, but Lilly also retained medical marketing firms and peer physicians paid by Lilly to promote Zyprexa as the comparative and safer choice both for on-label and off-label purposes. Lilly paid public officials who received "gratuities" or financial payoffs in order to foster Zyprexa usage and create faulty and misleading guidelines for antipsychotics usage. Lilly along with other drug manufacturers funded purported non-profit organizations with millions of dollars to lobby for the increased market share and marketing of atypical antipsychotics such as Zyprexa. Thus, Lilly associated itself with a discrete, identifiable

number of medical marketing firms, physicians, public officials and purported charities in order to effectuate the illegal and unlawful purposes of Zyprexa promotion, thereby masking Lilly's direct influence on the deceptive and misleading marketing and promotional campaign for Zyprexa.

5. The devastating consequences of Lilly's unlawful activities regarding the comparative efficacy, safety and off-label usage of Zyprexa resulted in both serious personal injuries to thousands of persons, as well as substantial and unnecessary economic burdens being placed on consumers and third party payors. The personal injury actions are addressed through other actions in this MDL. This Class Action Complaint seeks to address the economic harm suffered by consumers and third party payors.

6. Count I alleges a violation of the Racketeering Influenced and Corrupt Organizations Act ("RICO"), 18 U.S.C § 1961 (3). Lilly associated itself with a discrete and identifiable number of medical marketing firms, physicians, public officials and purported charities in order to form RICO associations-in-fact. These enterprises are described in this complaint as the Unlawful Zyprexa Promotion Enterprises. Through the use of these enterprises, Lilly engaged in a pattern of racketeering activity including at least multiple episodes of mail fraud and wire fraud. Consumers and third party payors were injured in their property by reason of these violations by, among other things, having to pay hundreds of millions of dollars for Zyprexa by reason of the unlawful conduct. Plaintiffs seek certification of a nationwide class, and treble damages on behalf of that class.

7. Count II alleges a conspiracy in violation of RICO under 18 U.S.C § 1962 (c). Lilly and its co-conspirators engaged in numerous overt and predicate fraudulent racketeering acts in furtherance of the conspiracy, and by reason of this conduct consumers and third party

payors were injured in their property. Plaintiffs seek certification of a nationwide class, and treble damages on behalf of that class.

8. Count III alleges a violation of state consumer protection law. As a direct result of Lilly's deceptive, unfair, unconscionable, and fraudulent conduct, consumers and third party payors were injured and suffered loss within the meaning of applicable and consumer protection statutes. Plaintiffs seek certification of a nationwide class (or group of classes) and applicable damages on behalf of that class.

9. Count IV alleges common law fraud.

10. Count V seeks relief in the nature of unjust enrichment. As a result of the intended and expected result of the conscious wrongdoings engaged in by Lilly, Lilly profited and benefited at the expense of the consumers and third party payors in the United States.

11. Finally, pursuant to Fed. R. Civ. P. 38, the First Amended Class Action Complaint seeks a jury trial on all issues so triable. Although these purchase claim proceedings are relatively young, given the pendency of this MDL for well over a year and given the interests of justice, proposed interim class counsel are prepared to proceed forward with discovery and a trial at a relative early date.

II. PARTIES

A. Plaintiff

12. Plaintiff Sergeants Benevolent Association Health and Welfare Fund ("SBA Fund" or "Plaintiff") is a citizen of the state of New York, and has its principal place of business at 35 Worth Street, New York, New York. SBA Fund is an "employee welfare benefit plan" and an "employee benefit plan." As such, SBA Fund is a legal entity entitled to bring suit in its own name. SBA Fund is a not-for-profit benefit fund, sponsored by and administered by a Board of

Trustees, established and maintained to provide comprehensive health care benefits to participant-workers, who are employed under various collective bargaining agreements, and to their dependents.

13. SBA Fund has paid all or part of the cost of its participants' purchases of Zyprexa during the Class Period, as defined herein. Pursuant to its plan, Plaintiff, through a pharmacy benefit manager and managed care administrator, purchased prescription drugs for its participants and provided coverage for medical testing and visits to physicians. Each plan participant has a prescription drug plan identification card which he/she presents at a participating pharmacy. Plaintiff has been injured as a result of the unlawful conduct of Defendant as alleged herein.

B. Defendant

14. Defendant Eli Lilly and Company ("Lilly" or "Defendant") is an Indiana corporation and has its principal place of business located at Lilly Corporate Center, Indianapolis, Indiana 46285. At all times relevant hereto, Lilly was engaged in the business of licensing, manufacturing, distributing, and/or selling, either directly or indirectly, through third-parties or related entities, the pharmaceutical prescription drug Zyprexa.

III. JURISDICTION

15. This court has subject matter jurisdiction pursuant to 28 U.S.C. § 1331, because this action arises under the laws of the United States, and 28 U.S.C. § 1964(c), because this action alleges violation of the Racketeer Influenced and Corrupt Organizations Act ("RICO"), 18 U.S.C. § 1962.

16. Plaintiffs also invoke jurisdiction pursuant to 28 U.S.C. § 1332 (d)(2), which provides federal district courts with original jurisdiction over civil actions in which the matter in

controversy exceeds the sum or value of \$5,000,000, exclusive of interest and costs, and is a class action in which “any member of a class of plaintiffs is a citizen of a state different from any defendant.”

17. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1391 (b) and (c), and 18 U.S.C. § 1965 because Defendant transacts business, is found, and/or has agents in this District, and because a substantial portion of part or all of the alleged improper conduct took place in this District. Lilly through its marketing and sales of Zyprexa has transacted substantial business in this District.

IV. FACTS

A. Federal Regulatory Background

18. The backdrop for the facts of this case, and in part the need for Lilly to conspire with others to effectuate its unlawful purposes, stems from two aspects of the federal regulatory regime for pharmaceutical products – the thresholds for FDA drug approval and the restrictions regarding off-label marketing practices.

19. Pharmaceutical companies must apply to the United States Food and Drug Administration (“FDA”) for approval to sell a new drug. When the FDA approves a drug product, it also approves the labeling that accompanies the drug. This labeling indicates the manner in which the product is to be used as well as the warnings that must be included with the product.

20. The label and the information provided by the manufacturer about its drug, including contraindications and potential side effects, are relied on by physicians in deciding a course of therapy for their patients. Although physicians are free to prescribe approved drugs as they see fit to treat any condition or symptom, pharmaceutical companies are prohibited from promoting drugs for uses outside of the approved labeling, commonly referred to as “off-label”

uses.

21. Strict federal laws and regulations also govern the required disclosure of adverse side effects associated with any prescription medication as well as the promotion and marketing of drugs for off-label uses.

22. Legal requirements for the content and format of drug labels, like Zyprexa, are codified in 21 CFR 201.57. Serious adverse reactions, which are potentially fatal, must be conspicuously warned of and cannot be buried in a drug's label. 21 C.F.R. 201.57, subsections (c) and (g) provide as follows:

(e) Warnings.

Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards....

The Labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with the drug; a causal relationship need not have been proved.

(g) (3) The 'Warnings' section of the labeling or, if appropriate, the 'Contraindications' section of the labeling shall identify any potentially fatal adverse reactions.

23. The regulations also obligate a drug manufacturer to advise prescribing physicians, and ultimately the patient, of the need to perform appropriate clinical testing and/or monitoring to prevent against foreseeable side effects from occurring. Subsection (f) of 21 CFR 201.57 states as follows:

The Precautions labeling shall contain the following:

(1)...any special care to be exercised by the practitioner for safe and effective use of the drug...

(3)...any lab tests that may be helpful in following the patient's response or in identifying possible adverse reactions...

24. The FDA regulates some aspects of the marketing and promotion of prescription

drugs. Under the Food Drug and Cosmetic Act, and the regulations promulgated thereunder, all information provided by a drug manufacturer about its products, whether on- or off-label, whether directed at consumer or physicians, must be fair and balanced. To be fair and balanced, information about a drug manufacturer's products must accurately and fairly represent all relevant data. In practice, this mean a drug manufacturer must present the positive as well as the negative information that it knows about the drug. Pharmaceutical companies may not present half-truths or disclose only select information favorable to their position. They must make full disclosure to meet their obligation of providing fair and balanced information. Lilly was aware of these requirements.

25. At all times relevant hereto, some aspects of Lilly's promotion of its products for off-label uses was also governed by some federal requirements. The general rule was that pharmaceutical companies could only promote their products for uses that had been approved by the FDA. Sales personnel could not discuss off-label uses with physicians during sales visits, and off-label uses were not supposed to be discussed in any promotional event sponsored by Defendant.

B. Schizophrenia and Traditional Antipsychotics

26. Schizophrenia is one of the most complex and challenging of psychiatric disorders. It represents a heterogeneous syndrome of disorganized and bizarre thoughts, delusions, hallucinations, inappropriate affect and impaired psycho-social functioning. Fortunately, schizophrenia is somewhat rare, occurring in only about 1% of the population.

27. There are many clinical presentations of schizophrenia. Despite common misconceptions of schizophrenia as a "split-personality", in fact schizophrenia is a chronic disorder of thought and affect. The Diagnostic and Statistical Manual of Mental Disorders, 4th edition, (DSM-IV) assigns a diagnosis of schizophrenia when a patient suffers two or more of the

following characteristic symptoms: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior and negative symptoms.¹

28. Although the etiology of schizophrenia is unknown, research has demonstrated various abnormalities in schizophrenic brain structure and function. The cause of schizophrenia is likely multi-factorial, that is, multiple pathophysiologic abnormalities may play a role in producing the similar but varying clinical phenotypes we refer to as schizophrenia.

29. Since the discovery of the effects of antipsychotics, such as chlorpromazine in the 1950s, and the observation that traditional anti-psychotic drugs are post-synaptic dopamine-receptor antagonists, the hypothesis has emerged that dopamine hyperactivity underscores the neurochemical basis for the primary symptoms of schizophrenia.

30. Over the years, treatment of schizophrenia has relied on antipsychotic drugs that target dopamine D2 receptors. The many antipsychotic drugs introduced during the following decades were increasingly potent, as medicinal chemists improved the drugs' affinity for the D2 receptor.

31. The traditional or "typical" antipsychotics include chlorpromazine (Thorazine), fluphenazine (Prolixin), haloperidol (Haldol), loxapine (Loxitane), molindone (Moban), mesoridazine (Serentil), perphenazine (Trilafon), thioridazine (Mellaril), thiothixene (Navanc), and trifluoperazine (Stelazine). Until the early 1990's, the typical antipsychotics were the common drug therapy for schizophrenia.

32. Although there were many traditional antipsychotics, the efficacy of these drugs was similar because they all had similar mechanisms of action. A troubling side effect of typical

¹ Only one of these criteria are required if delusions are bizarre or if hallucinations consist of a voice keeping a running commentary on the persons behavior or two or more voices conversing with each other. To achieve a diagnosis of schizophrenia, schizo-affective or mood disorder must be excluded, and the disorder must not be due to medical disorder or substance use.

antipsychotics was that the blockage of dopaminergic neurotransmission in the basal ganglia caused extrapyramidal syndromes (EPS) such as Parkinsonian effects. A long-lasting movement disorder, tardive dyskinesia, also occurred with prolonged treatment. And as to efficacy, the early promise that these drugs might dramatically improve patients' long term psychosocial and cognitive disabilities was only partially fulfilled.

33. By the 1980s, clozapine was being investigated for the treatment of schizophrenia on the theory that it might be more effective and cause less movement disorder than other antipsychotics. Clozapine was termed an atypical antipsychotic because it had an "atypical index" when measuring its effect on brain activity in different parts of the brain. It was hypothesized that the different effects by clozapine on the areas of the brain that control movement would cause less movement disorder than other antipsychotics. However, the potential of clozapine to cause toxic side effects, including agranulocytosis, limited its prescription to about 10 percent of persons with schizophrenia.

C. Emergence of the Atypical Antipsychotics or Second Generation Antipsychotics (SGA)

34. During the 1990's pharmaceutical companies, acting on the "atypical" hypothesis, introduced newer drugs attempting to capture the enhanced therapeutic effect of clozapine without its toxicity and without the increased EPS caused by traditional antipsychotics. Before 1993, the only atypical antipsychotic in the United States market was clozapine, and due to its toxicity it had very little market share. Ten years later, atypical antipsychotics such as Zyprexa would account for about 90% of all antipsychotic drugs prescribed for all psychiatric purposes, regardless of whether they were approved for those indications or not. The atypical antipsychotics include clozapine (Clozaril), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), aripiprazole (Abilify), and ziprasidone (Geodon), and are considered the

second generation antipsychotics (SGA). In part, this lawsuit describes how Lilly achieved, through a series of unlawful acts and practices, the largest United States market share for atypical antipsychotics, both for FDA-approved purposes and for unapproved purposes.

35. In late 1993, Risperdal became the first non-clozapine atypical antipsychotic to receive FDA approval. In early 1994, Janssen, a subsidiary of Johnson & Johnson, began marketing and selling Risperdal. During the next couple of years, Janssen heavily marketed and promoted Risperdal for its approved indication, management of the manifestation of psychotic disorders, and for multiple non-approved purposes of the drug, for example, attention deficit-hyperactivity disorder (ADHD), bipolar disorder, and aggression associated with late-onset dementia. By late 1996, Janssen had significant market share for United States antipsychotic drug use, and demonstrated the sales potential of marketing atypical psychotic usage for non-approved indications.

D. FDA Approval Process for Olanzapine

36. Meanwhile, in the early 1990's, Defendant Lilly developed and sought approval for its own atypical antipsychotic, olanzapine (the eventual trade name for which would be Zyprexa). Olanzapine is a selective monoaminergic antagonist with a high affinity binding to the subtypes of serotonin, dopamine and other receptors. Thus, as is the case with other antipsychotics, the proposed efficacy of olanzapine for schizophrenia is mediated through a combination of dopamine and serotonin type II (5HT₂) antagonism.

37. In seeking approval of olanzapine for the treatment of psychotic disorders, Lilly submitted two controlled studies showing olanzapine to be superior to placebo in the treatment of psychosis in patients with schizophrenia during short term (6 week) studies. As such, the FDA approval of olanzapine for the treatment of psychotic disorders constituted the regulatory minima traditional for FDA approval – olanzapine had been proven as better than nothing (i.e., a

placebo) during two short term (i.e., 6 week) studies. The FDA approval did not support, and did not constitute, an endorsement by the FDA that olanzapine was in terms of efficacy better than or equal to any other antipsychotic, traditional or atypical.

38. Moreover, the efficacy of olanzapine through two short-term (6 week) controlled trials was limited to inpatients who met the diagnosis criteria in the *Diagnostic & Statistical Manual of Mental Disorders, 3rd Edition, revised* (DSM-III-R) for schizophrenia. Thus, the original approved indication was limited to adults with psychotic disorders.²

39. Because the mechanisms of actions for olanzapine were fundamentally the same as other SGAs, the FDA required (and Lilly was constrained to acquiesce) to warnings for Zyprexa that included neuroleptic malignant syndrome (NMS) and tardive dyskinesia (TD).

40. Medical literature dating as far back as the 1950s, and Lilly's own pre-clinical studies of Zyprexa, demonstrated that Zyprexa, like older antipsychotic medications, had the potential to cause diabetes, diabetes-related injuries (e.g. weight gain and hyperglycemia), cardiovascular complications, and other severe adverse effects. By the time Zyprexa was first marketed, the neurochemical bases for the efficacy and side-effects were generally known to Lilly, i.e., effects on dopamine, serotonin, and histamine systems in the brain. Therefore Lilly should have been concerned about Zyprexa causing neurological problems, weight gain, diabetes, pancreatitis, hyperglycemia, cardiovascular complications, and metabolic syndrome. And yet Zyprexa's original label, and all label changes until 2004, did not adequately warn of these adverse effects.

41. Despite having been on notice of the potential for deadly diabetes-related side effects, Lilly opted for the bare minima of clinical trials, of limited duration, such that no side

² Although a single haloperidol arm was included as a comparative treatment in one of the two trials, this trial did not compare these two drugs over a full range of clinically relevant doses for both.

effects were likely to be revealed.

42. Despite knowing that Zyprexa increased the risks of weight gain, hyperglycemia, other adverse metabolic events, and certain cardiovascular issues, Lilly fought to keep fair and balanced disclosures regarding these risks from the Zyprexa label. During the FDA approval process, two important facts regarding the marketing of Zyprexa became apparent: 1) the need for restraint with respect to claims of efficacy, which according to the FDA had only been minimally demonstrated; and 2) Lilly's aversion to providing warnings about weight gain, much less the potential for diabetes. For example:

- In April 1995, researchers conducting statistical analysis of cardiovascular data from an earlier clinical study noted that although olanzapine dosing did not appear to affect cardiovascular signs, "[REDACTED]" ([REDACTED])
- In February 1995, Lilly executives met with FDA officials in a pre-NDA filing meeting to discuss research on olanzapine, including the patient populations being studied and for which approval would be sought. J. Alan Webber, in writing the results of the meeting, noted the FDA's warning about misleading statements regarding treatment of dementia: "[REDACTED]" In addition, the FDA warned Lilly about tactics and presentation of information about Zyprexa: "[REDACTED]"
- On August 3, 1995, Lilly prepared the "[REDACTED]" report to be submitted to the FDA with the NDA application. The summary included pre-February 14, 1995 safety data from approximately 50 completed and ongoing worldwide clinical studies, involving a total of 3201 patients, as well as a review of literature pertaining to the safety of olanzapine. A review of the "[REDACTED]" from the integrated database showed approximately 950 reported incidences of weight gain -- 30% of patients on olanzapine in those

clinical studies.

- A September 13, 1995 marketing presentation prepared by Adelphi International Research Limited highlights the "[REDACTED]" of Zyprexa as well as some of the "[REDACTED]" or side effects of the drug as compared to other antipsychotic drugs then offered. While the presentation notes that weight gain "[REDACTED]," it contains nothing on glucose monitoring or the potential health risks associated with significant weight gain brings. Instead, one "[REDACTED]" of Zyprexa was that patients on it required no blood monitoring, which was viewed as a "[REDACTED]". The slide touting this "benefit" states: "...

- On September 4, 1996, Lilly executives discussed the FDA's suggested changes to the Zyprexa draft labeling, disagreeing with the agency's proposal regarding the incidence of weight gain: "[REDACTED]"

" The FDA's recommended labeling notation on weight gain read as follows: "[REDACTED]"

" In addition to moving the paragraph to the "Adverse Reactions" section, Lilly also wanted to add a sentence: "[REDACTED]"

- On September 30, 1996, the FDA approved Lilly's NDA for Zyprexa, including draft labeling which was the result of several meetings and calls between the agency and Lilly during September 1996. The agency relented to Lilly's desire to move mention of weight gain to the "Adverse Reactions" section of the labeling and approved the following paragraph: "[REDACTED]"

[REDACTED]

43. In September of 1996, the FDA approved Zyprexa for use in the treatment of schizophrenia. Between that time and September 2003, there have been 17 different revisions to Zyprexa's product label. The dates of each revised product label are as follows: 10/2/96; 5/1/97; 8/11/97; 9/30/98; 11/19/98; 6/29/99; 3/17/00; 4/12/00; 8/3/00; 10/27/00; 2/16/01; 11/01; 3/5/02; 5/13/02; 1/24/03; 7/18/03; and 9/16/03. Between October 1996 and early-September 2003, Lilly never provided a prominent warning about the increased risk of diabetes and hyperglycemia and of the need to provide baseline diabetes screening and glucose monitoring until it was forced to do so by the FDA in mid-September of 2003.

44. Since Lilly introduced Zyprexa in 1996, it has been prescribed to more than twelve million people worldwide and became Lilly's top-selling drug. In 2003, approximately seven million prescriptions for Zyprexa were dispensed, resulting in more than \$2 billion in sales. Zyprexa was the seventh largest selling drug in the United States by retail sales in 2003. In 2004, Zyprexa sales exceeded \$4.4 billion.

45. Crucial to this blockbuster success was Lilly and its co-conspirators' aggressive marketing of Zyprexa, which consisted chiefly of overstating the drug's uses, while understating (if not outright concealing) its life-threatening side effects.

E. Lilly's Pre-Market Planning

46. Long before Lilly brought Zyprexa to an already well-established market for second-generation antipsychotics in September of 1996, Lilly had clearly set its strategy for the success of the new drug: to "[REDACTED]" and create research, with the help of paid, third party "[REDACTED]," that "[REDACTED]" establish Zyprexa as an effective and safe alternative to other similar agents, while downplaying and minimizing the drug's "[REDACTED]" and potential side

effects, and to promote Zyprexa as a drug that could be used for a broad array of "mood and thought disorder" symptoms, going far beyond the limited indication for schizophrenia that Lilly originally received from the FDA.

47. Prior to Zyprexa's FDA approval, Lilly had a well-developed strategy to expand the use of olanzapine beyond patients with schizophrenia. A 1994 presentation to the "[REDACTED]" outlined the team's mission, goals, and strategy for promoting utilization of the drug. The goals included ghost writing research and paying "[REDACTED]" to support Lilly's marketing aims. These "[REDACTED]" of course, were nothing more than third-party consultants and researchers who were put on Lilly's payroll to support and lend credibility to Lilly's scientific and marketing goals.

48. Among these goals were plans to "[REDACTED]"
[REDACTED]
[REDACTED]
[REDACTED]" while "[REDACTED]"
[REDACTED]" ([REDACTED]). Indeed, to begin the process of providing incentives and funding to doctors and researchers, Lilly planned to identify and meet with these "[REDACTED]" during the fourth quarter of 1995, approximately one year before Zyprexa came to market. ([REDACTED]) Lilly also trained its sales people as to how to "outline" or to even write articles for the doctors and in fact provided templates of articles that the doctors could submit under their own name. ([REDACTED])

49. Further, the "[REDACTED]" set out to "[REDACTED]"
[REDACTED]

[REDACTED]

[REDACTED]” ([REDACTED])

50. In a July 20, 1995 Zyprexa presentation again geared towards the “[REDACTED] [REDACTED],” Lilly estimated the schizophrenia drug market at approximately \$1 billion at the time, with “[REDACTED]” ([REDACTED]) Obviously, there was no possible way Lilly could have ever hoped to turn Zyprexa into drug that could seriously tap into this \$3.5 billion market by 2000 without marketing Zyprexa for a whole variety of off-label uses. Lilly’s global long-term marketing strategy in this regard is perhaps best summed up by the Zyprexa slogan it utilized in 1995: “[REDACTED] [REDACTED]” ([REDACTED])

51. In this regard, it was Lilly’s strategy well before the launch of Zyprexa to market the drug not only for use with children and the elderly but also for a whole variety of symptoms in the broad realm of “[REDACTED],” a strategy that gave rise to an ongoing pattern of false and misleading conduct in violation of not only FDA regulation but also state and federal fraud law.

52. From the outset, Lilly recognized the need to promote off-label uses as the key to blockbuster success for Zyprexa and included off-label uses in its long-term planning for the drug. For example, in another pre-launch internal strategy document entitled “[REDACTED] [REDACTED]” Lilly set a number of goals for itself prior to launching Zyprexa. One of the main goals identified in this strategy document was to “[REDACTED] [REDACTED]” The new and off-label indications identified by Lilly in this document included:

- “[REDACTED]”

([REDACTED])

55. Lilly was clear that its goal in examining the potential for Zyprexa was "[REDACTED]
[REDACTED]." As Lilly explained, [REDACTED]
[REDACTED]
[REDACTED]." ([REDACTED])

56. With such studies, however, Lilly was clearly interested only in what would
shower positive attention on the drug, as its strategy entailed having "[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]." ([REDACTED]) Thus, instead
of conducting research in good faith to legitimately test the efficacy and safety of olanzapine,
Lilly was more closely focused on creating narrowly tailored studies specifically designed to
"[REDACTED]." Such was the sales-first philosophy at Lilly, prior to the
launch of Zyprexa.

57. Lilly's clear aim from the outset was to expand the off-label indications for
Zyprexa despite the fact that its own pre-launch strategy documents pointed to and highlighted
numerous "drawbacks" of the drug, including:

- "[REDACTED]
[REDACTED]"
- "[REDACTED]"
- "[REDACTED]"
- "[REDACTED]"

([REDACTED])

58. Despite this knowledge, Lilly set out to aggressively market Zyprexa for the above-listed off-label uses and set further goals for itself, including:

- “[REDACTED]”
[REDACTED]
- “[REDACTED]”
[REDACTED]
- “[REDACTED]”
[REDACTED]
- “[REDACTED]”
[REDACTED]
- “[REDACTED]”
[REDACTED]
- “[REDACTED]”
[REDACTED]
- “[REDACTED]”
[REDACTED]
- Follow “[REDACTED]”

([REDACTED])

59. Thus, Lilly’s pre-launch commercialization plan was aimed at “[REDACTED]”
[REDACTED]” and undertaking “[REDACTED]”
[REDACTED]” such as efforts to “[REDACTED]”
[REDACTED]” “[REDACTED]” ([REDACTED]
[REDACTED])

60. Lilly, however, knew that it could not accomplish all these goals alone and was set on getting as much help as possible from third parties, such as paid “[REDACTED]” and from its “[REDACTED]”. As Lilly’s strategy documents state, in order to make Zyprexa succeed,

Lilly was prepared to "[REDACTED]
[REDACTED]" ([REDACTED].)

61. Prior to launch, Lilly also made certain to focus on positioning Zyprexa for maximum pricing and utilization. The 1994 "[REDACTED]" presentation noted two strategies on that front: "[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]" ([REDACTED].)

62. Indeed, in another pre-launch marketing strategy document, Lilly identifies a priority goal to "[REDACTED]" in 1996 and 1997. The number one priority goal of these "[REDACTED]" was to "[REDACTED]" ([REDACTED].) Another stated goal was to "[REDACTED]
[REDACTED]" ([REDACTED].) Thus, even at this early stage, Lilly's "[REDACTED]" approach to investigating Zyprexa was designed not to legitimately test for efficacy and safety, but instead to market to "[REDACTED]" and to "[REDACTED]
[REDACTED]" and maximize profits.

63. In short, Lilly's pre-launch marketing strategy for Zyprexa could be summarized as follows: result-driven study designs, which will be supported by result-driven selection of paid consultants and researchers, narrowly tailored such that they "[REDACTED]" only provide support for the efficacy and safety of Zyprexa as an agent capable of combating as wide a variety of disease states and symptoms as possible - and going far beyond the limited indication for psychotic

disorders originally obtained from the FDA – so that Lilly could sell as much of this drug to as many patients at the maximum price possible, despite the known “[REDACTED]” of the drug.

F. Formation of the Lilly Unlawful Zyprexa Marketing Enterprises

64. Beginning in 1996 and continuing to the present, Lilly implemented a marketing, advertising and promotion campaign by combining its own significant personnel and financial resources with a discreet and identifiable number of medical marketing firms, peer physicians, public officials and purported charities through which Lilly (i) falsely and deceptively oversold the efficacy of Zyprexa as compared to other antipsychotics, (ii) failed to adequately warn of, and affirmatively mislead the medical community regarding the severe side effects of Zyprexa such as weight gain, hyperglycemia, diabetes and cardiovascular effects, and (iii) unlawfully promoted Zyprexa for usage in populations for which it had not received FDA approval and for which the efficacy and side effects had not been established through adequate clinical evidence. These associations-in-fact created by Lilly are denominated in this complaint as the Zyprexa Unlawful Marketing Enterprises. Lilly established these enterprises to accomplish several goals instrumental to a scheme to market Zyprexa through fraudulent, or false and deceptive, claims of efficacy and safety, and for unlawful, off-label purposes.

65. First, Lilly had to create parallel marketing structures that appeared independent from Lilly’s ordinary promotion forces – it did so both to avoid federal regulations concerning off-label promotion and to create the façade of independence behind the misleading messages of safety, efficacy and non-indicated usage it wished to promote.

66. Second, to execute successfully its publication strategy, favorable articles had to be generated and published that appeared to emanate from independent physicians, and continuing legal education marketing schemes needed to flood the information market, all of which would give the appearance of independent peer-to-peer credibility.

67. Third, given the predominant usage of antipsychotics in the public sector (primarily Medicaid because of the high population of mentally ill in the Medicaid eligible demographic), to be successful in its unlawful promotional efforts, Lilly corrupted thought leaders in state public agencies to use, and indeed have themselves promote, atypical antipsychotics, including Zyprexa.

68. All of these goals were complimentary and mutually reinforcing. The production of favorable publications helped create a "██████" regarding Zyprexa: peer-to-peer marketing and promotion allowed aggressive sales pitches to continue with the veneer of legitimacy; state public officials were co-opted to promote and over utilize atypical antipsychotics such as Zyprexa and all these effects would spill over to other state Medicaid agencies and to private payor networks.

69. To achieve all these goals, Lilly entered into three sub-enterprises: the Peer-Selling Enterprise, the Publication-Enterprise, and the Public Payor-Enterprise.

1. Peer-Selling Enterprise

70. Defendant's peer-to-peer marketing scheme centered on hosting numerous events where doctors trained and/or approved by Lilly would falsely oversell the efficacy and safety of Zyprexa and would provide favorable information on the off-label use of Zyprexa, often under conditions where physicians would be compensated for attending the presentation. Defendant funded scores of such events between 1996 to present. Because Lilly was prohibited from directly producing such events, it created and controlled a Peer-Selling Enterprise composed of medical marketing firms (the "vendor participants") and several dozen physicians (the "physician participants") who routinely promoted Zyprexa to other physicians in venues all across the country. Defendant maintained sufficient control over the enterprise to select and approve the content of the programs and the physician participants that would deliver the off-

label message. The physicians who attended these events were deceived into thinking that the events were educational in nature and independent from the control of the Defendant.

71. The Peer-Selling Enterprise employed improper and unlawful sales and marketing practices, including: (a) deliberately misrepresenting the safety and medical efficacy of Zyprexa for a variety of off-label uses; (b) knowingly misrepresenting the existence and findings of scientific data, studies, reports and clinical trials concerning the safety and medical efficacy of Zyprexa for both approved indications as well as a variety of off-label uses; (c) deliberately concealing negative findings or the absence of positive findings relating to Zyprexa's and/or its off-label uses; (d) wrongfully and illegally compensating physicians for causing the prescribing Zyprexa; (e) knowingly publishing articles, studies and reports misrepresenting the scientific credibility of data and touting the medical efficacy of Zyprexa for both on-label and off-label uses; (f) intentionally misrepresenting and concealing Defendant's role and participation in the creation and sponsorship of a variety of events, articles and publications used to sell Zyprexa to off-label markets; and (g) intentionally misrepresenting and concealing the financial ties between Defendant and other participants in the Enterprise.

72. Defendant's scheme reaped it significant financial gain. From 1995 to 2004, Defendant's revenues from the sale of Zyprexa soared into the billions. By 2003, about 50% of all Zyprexa prescriptions were for off-label uses. Sales of the drug have grown at a significant rate each year.

73. All of the participants in the Peer Selling Enterprise associated with Defendant with the common purpose of aiding it in marketing Zyprexa for off-label uses and to achieve "market expansion" of these uses. Each of the participants received substantial revenue from the scheme to promote Zyprexa off-label. The more successful these marketing events were, the

more events there would be in the future and the more fees each of the participants would receive for participating in the events. For these reasons, all of the participants knowingly and willingly agreed to assist Defendant in its off-label promotion of Zyprexa, notwithstanding the fact that such a promotional campaign required the systematic repetition of false and misleading statements to, and the commercial bribery (through kickbacks) of, a score or more physicians throughout the United States, and that the promotion of Zyprexa for off-label indications by Defendant was illegal.

74. Lilly controlled the Peer Selling Enterprise. It compensated the other participants for their efforts, and controlled the money flow to the participating vendors and physicians. Lilly closely monitored all events to insure the expected representations related to off-label Zyprexa were made to physicians attending the events.

a. Role of Medical Marketing Firms in Peer-Selling Enterprise

75. Third party medical marketing firms were critical to Lilly's scheme to promote Zyprexa off-label from the scheme's inception. Lilly's marketing plans called for off-label information concerning Zyprexa to be widely disclosed in continuing medical education programs, "consultants' meetings", and other programs where physicians could instruct other doctors how to use Zyprexa for unapproved indications. Bona fide continuing medical education programs and similar educational events were exempt from FDA rules prohibiting off-label promotion because the sponsoring organization—which was often a nonprofit, like a medical school, was independent and was supposed to control the programs' content. In practice, however, these programs were produced with the assistance of third party medical marketing firms, and these firms supplied content and controlled the selection of presenting physicians.

76. Lilly's marketing strategies turned the proper practices for presenting continuing medical education programs on their head. Instead of accredited institutions planning

independent programs and then approaching third party vendors and financial sponsors, Defendant intended to create turnkey medical programs, with financing already included, and then find "independent" institutions that would present the package in the format Lilly and its enterprise created.

77. Among the information the Defendant, the participating vendors and the participating physicians deliberately omitted from the events they sponsored was the following:

- the lack of clinical trial evidence to support Zyprexa's off-label uses;
- negative clinical trial results that demonstrated that Zyprexa was no more effective than other, less costly, medications;
- negative evidence that Zyprexa did not work for off-label conditions;
- information that virtually all publications and studies that allegedly supported Zyprexa's off-label use had been funded by Defendant;
- information that virtually all publications and studies that allegedly supported Zyprexa's off label use had been initiated by Defendant pursuant to a corporate marketing plan designed to increase off-label sales;
- information that the participating doctors who were conducting the peer selling had been paid substantial subsidies to use Zyprexa on their patients for off-label purposes;
- that the events the physicians were attending were neither fair nor balanced and were created to insure the physicians would not hear a fair and balanced examination of Zyprexa for off-label uses;
- information that the events were not funded, as advertised, by an "unrestricted" grant from the Defendant, but that the grants were conditioned upon the

participating vendors and sponsoring institutions putting on presentations that painted the off-label use of Zyprexa in the most favorable light; and

- information with respect to dangerous side effects revealed through Lilly's internal research, adverse event reports, and independent research.

78. Each of the participating vendors was in regular communication with the Defendant. In connection with major medical congresses or conventions of the specialists that were the target of the off-label promotion campaign, the participating vendors coordinated their events to ensure their off-label message reached the most physicians in the most effective manner. All of the participating vendors were also in regular communication with the participating physicians, and individual participating physicians would give the same presentation (or a substantially equivalent presentation) at different participating vendors' events.

79. The planning and coordination of all of these events by the third party medical marketing firms required extensive use of the wires and mails, including the mailing of invitations to physicians, the mailing of proposals to the accrediting institutions, booking of hotels and airplane tickets, the arrangement of meals, the scheduling of teleconference calls, the development and modification of the tactical plans, and the coordination of the content of the presentations on Zyprexa to be presented at the event.

80. Firms that participated in the Peer Selling Enterprise include third party advertisers, proliferation firms and outside consultants such as Creative Street, Inc; Marketplace Management; Lewis & Gore; Harper; Aldephi Research, Millward-Brown Research; GSW; Pramaton, Inc.; Martin Hamblin; Cohn & Wolfe; and Grey Strategic Marketing/Grey Healthcare Group.

b. Role of Physicians

81. One of Lilly's principal strategies for marketing Zyprexa was to target key

physicians to serve as thought leaders. These doctors would promote Zyprexa to their peers through peer selling programs by (i) touting Zyprexa's supposed off-label uses; (ii) claiming that Zyprexa was being widely used by other physicians for off-label uses; (iii) suggesting mechanisms of action that could explain Zyprexa's efficacy, safety profile and use in off-label areas, even though the mechanism of action in any area was not, and still is not, understood; and (iv) claiming that they were privy to the latest clinical data that had not been released yet, but which would support off-label use.

82. To lure physicians to participate in the Peer Selling Enterprise, Defendant approached target doctors and informed them of the Defendant's interest in funding research opportunities and clinical trials at their institutions. Doctors who were willing to speak favorably about Zyprexa could likely receive substantial funds in the form of research grants. Lilly instructed its sales departments to select doctors at the major teaching hospitals to become "Zyprexa experts" who would in turn deliver the Zyprexa message to other physicians to grow Zyprexa sales. This could be done formally to other physicians at marketing events or informally to colleagues within a hospital or medical practice.

83. Having recruited these physicians, the Peer Selling Enterprise created an explosion in the off-label use of Zyprexa by artificially creating the perception that physicians were clinically using Zyprexa and investigating its efficacy in off-label uses on their own initiative, and not as a result of the illegal marketing activities. Defendant developed a stable of physicians to create this perception. Defendant, principally through the vendor participants, paid these physicians to induce them to write journal articles and letters to the editor that favorably discussed the off-label use of Zyprexa. Defendant also paid these physicians (in addition to providing free travel to resorts, free lodging and free meals) to induce them to give talks at

medical education seminars, advisory boards, consultants' meetings, speakers bureaus and similar events that favorably discussed the off-label uses of Zyprexa. The physicians who accepted these benefits and agreed to promote Zyprexa off-label to other doctors were physician participants in the Peer Selling Enterprise. The individual physician participants received tens of thousands of dollars to promote Zyprexa's off-label uses.

84. Physician participants were absolutely critical to the success of the Peer Selling Enterprise and all of the marketing plans drafted by the Defendant and the vendor participants required their participation. The participation of physicians allowed the Defendant and vendor participants to disguise promotional events as educational events or consultants' meetings. Moreover, as noted above, the Defendant and vendor participants knew that peer-to-peer selling was far more persuasive than traditional detailing. By funneling the payments to the physician participants through the vendor participants, the Enterprise could hide the speakers' financial ties with the Defendant, the Enterprise was able to mislead physician-listeners into believing that the speakers were not biased and that the events were not promotional. The large amounts of money the participating physicians received from the Defendant, for speaking and other purposes, was hidden from the physicians who attended events at which the participating physicians spoke.

85. Some physicians participated in the Peer Selling Enterprise by publishing favorable journal articles and letters to the editor about off-label use of Zyprexa. Defendant paid large sums of money, often in the form of research grants, to the physician participants in order to publish such articles. In some cases, the physician was not required to perform any research or even write the article. Marketing firms who were financed by the Defendant ghostwrote articles under the physician participants' names. Physicians merely had to "lend" their names to the articles, in exchange for a payment.

86. Physicians who participated in the Peer Selling Enterprise, either as speakers or as authors, entered into a mutually advantageous relationship with the Defendant. The more favorable a physician's statements were, the more he or she could expect to receive in the form of speaker fees and research grants. Physicians who refused to deliver the favorable off-label message that the Defendant wanted were blackballed and would not receive additional payments.

87. The participating physicians knew that minimal scientific evidence supported the use of Zyprexa for the off-label uses and that the type of clinical evidence that existed was insufficient, under the usual standards in the medical profession, to represent that Zyprexa worked for the unapproved indications.

88. Physician participants worked with, and were retained by, multiple vendor participants. All of the physician participants also had personal relationships with employees of the Defendant, frequently Defendant recommended specific individual participants for events.

89. Some of the physicians that participated in the Peer Selling Enterprise included Dr. Peter Haddad; Dr. William Carter; Dr. Jorge Falero; Dr. Lyle Torguson; Dr. John Buse; Dr. Robert Smith; Dr. Sumer Verma; and Dr. Rory Holman.

90. Plaintiffs do not at this time know the identity of all of the physician participants. The Zyprexa Unlawful Marketing Enterprise sponsored hundreds of events across the country between 1996 and 2004 and the Plaintiffs have only had an opportunity to review the records of a small subgroup of these events. Based on the records reviewed to date, at least one dozen individual physician participants, received \$25,000 or more for participating in the Zyprexa Unlawful Marketing Enterprises' activities for the time period indicated below (not counting travel, food, lodging and entertainment benefits they received for events held at resorts or out of town hotels).

c. Role of Pharmacies

91. Another of Lilly's strategies for marketing Zyprexa was to target pharmacies. One vehicle of choice was the pharmacies that serviced long term care facilities. Lilly set up a separate sales division to service the long term care facilities because those facilities encompassed the elderly population as well as children who are treated for behavioral symptoms, both of which Lilly saw as prime target populations for Zyprexa's off label growth. Not surprisingly, the growth of sales in the long term sales division was heavily weighted to pediatric use, all of which was off label, and to off label uses in the elderly population.

92. Long term facilities are not serviced by traditional retail pharmacies. Instead they are serviced by "closed end" pharmacies that service only long term facilities. The long term care pharmacy market is dominated by a few companies, including Omnicare, Pharmerica, and Neighbor Care. Thus the long term care sales representative worked very closely with the long term care pharmacies in marketing Zyprexa off label to physicians. Lilly sales representatives often used unrestricted educational grants to effectuate their off label scheme with the pharmacies.

93. A Lilly sales representative and a pharmacy would agree that the pharmacy would request funding from Lilly in order to present an educational program. The amounts of the educational grants would vary but would be for thousands of dollars. For instance, the sales representative and the pharmacy might agree that the pharmacy would present an educational program for the treatment of dementia. Both the pharmacy and the Lilly sales representative would agree that the program would include a presentation for the off label use of Zyprexa to treat dementia. The Lilly sales representative would then recommend a doctor who Lilly knew would make a presentation on the off label use of Zyprexa for dementia.

94. The Lilly sales representative would then file a form with Lilly headquarters in

Indianapolis requesting that a check be issued to the pharmacy for an educational grant. Lilly headquarters would issue the check in the name of the pharmacy. The pharmacy would then issue a check to the doctor making the presentation. Since the pharmacy theoretically “controlled” the presentation, Lilly considered it a “[REDACTED]” event that could contain off label information without running afoul of FDA regulations on off label marketing.

95. Each sales representative in the long term care sales division had a quarterly budget of approximately \$10,000 to request unrestricted educational grants from Lilly headquarters. Thus Lilly headquarters was able to use the unrestricted grants to funnel a constant flow of money to all parts of the country for purposes of off label marketing to the long term care market of elderly and children populations.

96. Lilly’s off label pharmacy scheme may have not escaped detection of the federal government. Lilly recently announced that, in October of 2005, the United States Attorneys Office in the District of Massachusetts issued a subpoena to Lilly seeking documents relating to Lilly’s business relationship with a long term care pharmacy and Zyprexa.

97. The long term care division was ultimately shut down by Lilly when it was merged with the hospital sales division in or about June of 2003, which is about the time that Lilly acknowledged the existence of ongoing federal investigations into Lilly’s off label marketing activities. Lilly did also ultimately sever the educational grant request process from its sales force.

2. Publication Enterprise

98. In order to execute their publication strategy, Defendant also needed to generate favorable articles about Zyprexa’s off-label uses. However, Defendant’s apparent control of this strategy had to be kept to an absolute minimum. Articles had to appear as if they emanated from

independent physicians who were investigating Zyprexa independently. To perform these tasks Defendant established a sub-enterprise of the Zyprexa Unlawful Marketing Enterprises, which would create "independent" publications. Like the Peer Selling Enterprise, the Publication Enterprise was an association in fact of medical marketing companies, participating physicians and Defendant, for the purpose of promoting off-label uses of Zyprexa. Alternatively, the Publication Enterprise can be viewed as an enterprise which was separate and distinct from the other Zyprexa Unlawful Marketing Enterprises.

99. Defendant's "publication strategy" required publications from independent physicians when in fact no such publications existed. Defendant created the Publication Enterprise to hire non-physician technical writers to create the necessary articles and then paid actual specialists to be the articles' "██████." This practice is referred to as "██████."

100. In order to monitor the status of publications, and in order to coordinate and execute the ghostwriting plan, marketing firms were necessary. The role played by the firms in assisting the Defendant in creating publications was very similar to the role played by marketing firms in the coordination of peer-to-peer marketing events.

101. Publications that Defendant distributed as part of their "publication strategy," intentionally misrepresented Defendant's role in the creation and sponsorship of the publications. Physicians who reviewed these publications were led to believe that the publications were the independent, unbiased research of the authors of the articles. They were not made aware of the fact that Defendant had in fact solicited these articles or that they had paid significant sums of money in various forms to the physician authors to induce them to make favorable statements about Zyprexa.

102. Even in cases where physician-authors drafted the articles themselves, they did so

under the same system of direction and control through which Defendant controlled speaker content. Physicians were promised grants and other gifts if they wrote favorable articles. If a physician attempted to write a negative article, Defendant would attempt to intervene and have a more favorable draft written. If this failed, Defendant would do their best efforts to suppress the article or restrict its dissemination.

103. For example, on May 14, 2003, Dr. John Buse of the University of North Carolina wrote to the editor of Diabetic Care and complained about an article that represented the "[REDACTED]" of one of Lilly's competitors. Among other things, Dr. Buse was concerned that the article – written by "[REDACTED]" – helped a competitor's "[REDACTED]" [REDACTED]

[REDACTED].” ([REDACTED]) Dr. Buse gave partial disclosure of his own corporate affiliations: “[REDACTED]” [REDACTED]” He did not reveal that he and/or his Department had received honoraria, grants, travel expenses, and/or other monetary benefits from his affiliation with Lilly. In an ironic comment about the unfavorable article published in Diabetic Care, Dr. Buse noted “[REDACTED]” [REDACTED]

[REDACTED].” His comment revealed as much about the inner workings of Lilly's Publication Enterprise as it did about this particular article. In a subsequent email correspondence with the editor of Diabetic Care, Dr. Buse attempted to cast dispersion on the results of the published article, noting “[REDACTED]” [REDACTED]

[REDACTED]” ([REDACTED])

104. Even though he called himself an "[REDACTED]", Dr. Buse elsewhere acknowledged the financial benefit that his medical department received from Lilly: "[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]" ([REDACTED]) Dr. Buse had plenty to gain from Lilly's funds. They were used for research and other purposes to help Dr. Buse conduct studies, publish articles, and make presentations that helped him as an "[REDACTED]" to reach the goal of tenure.

105. The final method by which Defendant controlled the stream of published information was through its policy of publishing only favorable results of its own internal trials and suppressing results that were unfavorable. In the case of an early trial that failed to show Zyprexa's efficacy for migraine, the results were never published. In the case of a clinical trial that failed to show Zyprexa's efficacy for bipolar disorder, the publication of results was delayed until the patent life was set to expire, and even then, Defendant never forwarded a copy of the article to DRUGDEX.

106. Although Plaintiffs are aware of the policy of suppressing unfavorable studies because of the express terms of the corporate decisions implementing the Publication Strategy, all information regarding negative studies funded by Lilly remains in the sole possession of Lilly and/or members of the Zyprexa Unlawful Marketing Enterprises. Without access to records of the studies that were funded and the results of those studies, Plaintiffs cannot identify specific negative findings. Defendant has never produced the results of these studies to the public or to

the Plaintiffs and their attorneys.

3. Public Payor Enterprise

107. Beginning in the 1990's and continuing to today, Lilly and other atypical antipsychotic drug manufacturers employed a strategy to capture Medicaid and Medicare markets that involved a focus on a relatively small group of customers – state officials who oversee treatment for many people with serious mental illness. These patients are found in state mental hospitals and state mental health clinics and are on Medicaid, and they are among the largest users of antipsychotic drugs.

108. Lilly entered into agreements with state public officials in, among others, Texas, Tennessee, Pennsylvania and Ohio, paying them substantial sums of money. Lilly directly and indirectly worked with and controlled certain state officials, enlisting them in an ongoing course of conduct to spread falsehoods regarding the efficacy, safety, and side effects of Zyprexa and to promote its off-label use.

109. In addition to influencing and corrupting state officials, Lilly influenced prescribing physicians to over-medicate senior citizens in nursing homes with antipsychotics. The use, as much as about 75% of the long-term care elderly residents in various demographic areas have received psychotropic medications. Lilly also influenced prescribing physicians to over-medicate adolescents in detention centers and other institutions.

G. 1996-2000: Launch of Zyprexa and Operations of the Unlawful Marketing Enterprises

110. Following the September 30, 1996 approval of Zyprexa by the FDA for the treatment of schizophrenia and despite this limited approval market, in eight years, Zyprexa has grown to become the third best-selling drug in the world. In its first full year of sales, Zyprexa's worldwide sales were \$500 million dollars in revenue. In 2004, worldwide Zyprexa sales

exceeded \$4.4 billion.

111. To achieve such massive sales, for a drug intended to treat an admittedly small market, Lilly, through the use of an enormous sales force and very aggressive marketing techniques, deliberately over-promoted Zyprexa to physicians and patients for symptoms and indications that were completely unrelated to schizophrenia (and, later, to bipolar mania). A Lilly internal email generated in 2001 boasted "[REDACTED]
[REDACTED]
[REDACTED]." ([REDACTED])

112. The over-promotion of Zyprexa by Lilly was a deliberate and calculated campaign designed to increase sales of the drug without regard for the safety of patients. The campaign also sought to distinguish Zyprexa as expensive but well worth the extra cost given its efficacy – which Lilly claims keeps schizophrenia patients out of the hospital more often than their competitors' drugs. (Lilly 10-Q (Nov. 3, 2005))

113. This over-promotion was not the action of an over-zealous sales force. Rather, Lilly's executives in the US and other countries, along with its scientists, marketing executives, medical staff and hired consultants and subsidiaries all worked together to develop, implement and carry-out this well-designed strategic marketing campaign.

114. The campaign was closely supervised. Every Lilly-sponsored research paper, clinical study, sales representative training session, physician education luncheon and press release was crafted to further the campaign. The control exercised by Lilly over its marketing campaign was most apparent when outside forces began to affect Zyprexa sales. As reports of diabetes and weight gain related to Zyprexa began to escalate, Lilly carefully responded with focused papers and articles, physician-targeted educational seminars, and letters, even when the

“new” message contradicted earlier messages.

115. The sales force was taught how to react to every question and concern in a way that furthered the campaign. During the early years, representatives were taught to ignore, dismiss or evade questions concerning weight gain and hyperglycemia. Later, representatives were taught to acknowledge these side effects but to emphasize that they were present in all schizophrenic medications and a likely consequence of the mental disease itself. Neither position was supported by studies but rather was conceived to lessen any impact of the truth about the serious side effects on sales.

1. Fraudulent and Unlawful Acts Regarding Safety and Efficacy

116. When presenting off-label information about Zyprexa to physicians in response to unsolicited requests for information on unapproved uses, Defendant was required to provide fair and balanced information. Defendant was also required to provide fair and balanced information whenever it engaged in promotional activities. Fair balance was not limited to written materials but all presentations. Defendant knew that whenever they were required to provide fair and balanced information, federal law and industry standards required them to provide any negative information as well as positive information about their drug products.

117. Within the medical community, in the context of describing properties of approved prescriptions drugs, the terms “effective” and “efficacy” have specific and well understood meanings. Because the FDA will only find a drug product to be effective if the proposed use is supported by well designed, placebo-controlled clinical trials that establish a causal relationship to a statistically significant degree, a statement that a drug is “effective,” or “works,” or “has been proven to . . .” is understood to mean that well controlled clinical studies support the use. To make such a statement without such clinical trial proof is misleading. Further, failure to inform physicians that no placebo-controlled clinical trials support a

representation of drug efficacy is a violation of a pharmaceutical company's obligation to disclose.

118. Although Defendant has extensively promoted Zyprexa for off-label purposes, few placebo-controlled, clinical studies have been conducted on off-label uses of Zyprexa. Most of those that have been conducted were negative or inconclusive. Placebo controlled clinical trials for Zyprexa's use for bipolar disorder, unipolar disorder, essential tremor, spasticity, controlled diabetic pain, and panic disorder have all failed to show that Zyprexa is effective for those conditions. Any presentation concerning Zyprexa's use for indications other than those approved by the FDA that purports to rely on clinical or published evidence must also describe those clinical studies that have found that Zyprexa is not effective for off-label uses. Where such information is not provided, any statements about Zyprexa's effectiveness for off-label use is false, misleading, distorted, inaccurate, unfair, imbalanced and omits material facts necessary to be disclosed.

119. In a February 14, 2000 Lilly document entitled "[REDACTED]", a list appeared of the Lilly-sponsored programs throughout 1999 that specifically "[REDACTED]". These programs included symposia and audioconferences and involved at least 40 cities. ([REDACTED])

120. An example of one Lilly presentation stated:

Limitations of Conventional Antipsychotic Medications

- Conventional antipsychotics fail to
 - Correct primary disorders of thought
 - Alleviate negative symptoms or associated depression
 - Arrest disease progression
- Conventional antipsychotics cause
 - Extrapyramidal dysfunction/tardive dyskinesia
 - Sedation/cognitive impairment
 - Effects on cardiovascular system, sexual function, and blood components
- Approximately 50% of patients do not respond adequately to conventional antipsychotic drugs
- Noncompliance rates, in part attributable to drug side effects, are excessively high and contribute to relapse

The disadvantages of conventional antipsychotic agents are well documented. These drugs are often ineffective or only minimally effective against the positive symptoms of schizophrenia, and do not affect negative or depressive symptoms or disease progression. Moreover, therapy with conventional antipsychotic drugs is often hampered by significant adverse reactions, both because of their effects on overall health and because of their impact on compliance. As many as half of schizophrenics who are treated with conventional antipsychotic medications do not achieve an adequate response.

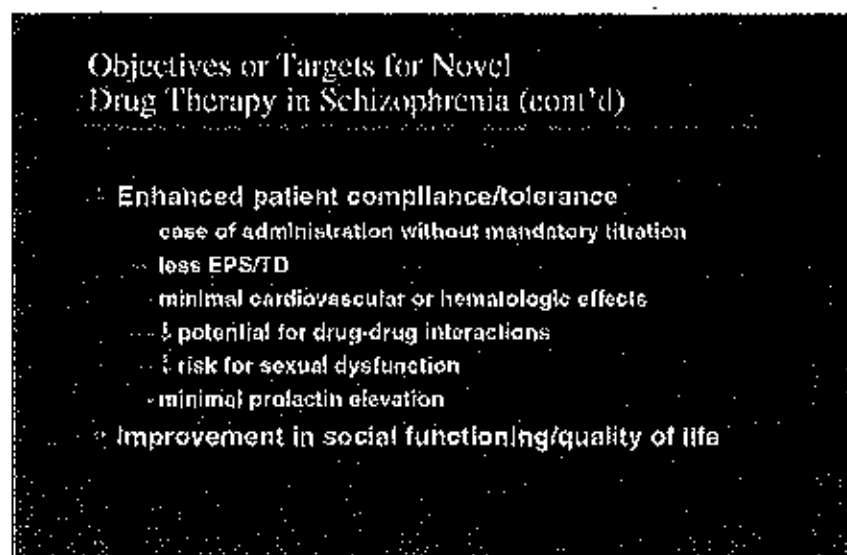
121. Another stated:

Objectives or Targets for Novel Drug Therapy in Schizophrenia

- Treatment for partial or non-responsive patients
- Efficacy against positive, negative, and comorbid mood symptoms
- Restoration or protection against further cognitive decline
- Effective maintenance and reduced rehospitalization rates
- Improved quality of life and hope for reintegration

The availability of a new generation of antipsychotic medications represents new hope for effective treatment, even for patients who have been refractory to conventional drugs. Enhanced efficacy would mean improvement in all categories of symptoms as well as protection against disease progression. And, patients who are effectively maintained on medication without rehospitalization have better opportunities for reintegration into society.

122. Yet another noted:



Patients are always more likely to be compliant with regimens that are easy to tolerate and that do not negatively affect quality of life. Likewise, compliance is generally better with drugs that do not require complicated titration and administration schedules. Unlike the dubious benefits of conventional agents, which often appear to have high price tags in terms of side effects and quality of life, the new generation of antipsychotic drugs is likely to offer patients a real chance at improved function and more normal lives.

123. One presentation stated:

Schizophrenia: Typical vs Atypical Antipsychotic Agents

	Typical Antipsychotics	Clozapine	Risperidone	Olanzapine	Quetiapine
Positive Symptoms	++	++	++	++	++
Negative Symptoms	--	+	+	+	+
EPS	↑↑	--	Dose- related risk	--	--
Prolactin Elevation	↑↑	--	↑↑	--	--

EPS = extrapyramidal symptoms
 ++ = very effective, + = effective, -- = no effect, ↑↑ = high risk

124. Federal law and industry standards also prohibited Defendant from misrepresenting scientific evidence that supported (or failed to support) claims that a drug was effective for a specific condition. Thus, anecdotal evidence of a drug's usefulness for a given condition could not be presented as the equivalent of the findings of a well-designed clinical trial. To fail to comply with these standards violated the Defendant's legal duty to provide accurate and non-misleading information.

125. In addition to its failure to warn of the serious and life-threatening illnesses associated with their drug Zyprexa, Defendant also undertook, through the use of intermediary marketing firms, to promote the use of Zyprexa for uses for which it was never approved by the FDA and for which it has never been proven to be safe or effective. This is known as off-label use.

126. In order to gain additional sales and to compete with other antipsychotics such as Risperdal, Lilly undertook a scheme to market and promote Zyprexa for off-label purposes,

including for use in the treatment of children and adolescents, "soccer moms", and the elderly. Lilly also devised a campaign to market primary care physicians [PCPs] that was used to educate them about the patients in their practices whose symptoms might suggest Zyprexa use, albeit off-label.

127. Defendant employed the services of various third-party marketing firms in order to effectuate their scheme to market Zyprexa for these off-label purposes. These firms undertook the marketing of Zyprexa for off-label uses at the discretion and control of Defendant. The rise in the use of Zyprexa for off-label use is a well documented phenomenon. The promotion of Zyprexa by Defendant and the intermediary marketing firms working with Defendant to promote Zyprexa for off-label uses account in large part for the meteoric rise in Zyprexa sales and in the income derived by Defendant for sales of Zyprexa.

128. Lilly understood that off-label use of Zyprexa was the key to increased sales. Lilly not only promoted off-label use, it carefully tracked Zyprexa's progress in these markets. On June 9, 2004, Lilly presented a powerpoint slide show entitled, "[REDACTED]". At slide 44, Lilly presents a breakdown of national sales data (source listed as NDTI 2001)) on Zyprexa use by diagnoses: "[REDACTED]". By at least 2001, Lilly knew that half of its sales were for non-approved uses. ([REDACTED])

129. For each patient and physician population, a separate marketing campaign was developed in conjunction with various third-party marketing firms with accompanying promotional materials, educational seminars, training sessions, "[REDACTED]", and timely Lilly-sponsored published research and opinion papers.

130. The Zyprexa Unlawful Marketing Enterprises routinely and knowingly provided false, inaccurate, misleading, distorted, unfair and unbalanced information about Zyprexa's use for unapproved indications. Without discovery, Plaintiffs cannot catalog each misrepresentation and/or misleading statement about Zyprexa because Plaintiffs do not possess all transcripts of all meetings. The vast majority of these transcripts is in the possession of the Defendant and/or other members of the Zyprexa Unlawful Marketing Enterprises and has not been produced for the Plaintiffs.

2. Fraudulent and Unlawful Acts Regarding Off-Label Promotions for Elderly Usage

131. From Zyprexa's launch, Lilly's marketing campaign included promotion of the drug for use in the elderly for both dementia symptoms and Alzheimer's disease. This off-label marketing promotion is particularly sinister given the results of a study performed by Lilly in 1995, before Zyprexa was even approved. Lilly learned that olanzapine was ineffective in treating such conditions as dementia and Alzheimer's. In the summary section prepared on August 7, 1996 of study F1D-MC-HGAO, Lilly stated that "[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]." ([REDACTED]
[REDACTED]) Nevertheless, Lilly promoted Zyprexa for symptoms of dementia and Alzheimer's in the elderly from the product's inception.

132. On February 16, 1995, Lilly met with FDA officials to discuss research on olanzapine in elderly and adolescent patients. In internal notes prepared by Lilly concerning this meeting, Lilly indicates that it was warned about misleading statements concerning the use of Zyprexa for the elderly:

[REDACTED]

([REDACTED]) The notes also describe how the FDA went on to warn Lilly to be honest about its data for Zyprexa: "[REDACTED]"

[REDACTED]

[REDACTED] " ([REDACTED])

133. In spite of the FDA's admonitions, Lilly promoted off-label use of Zyprexa for the elderly to nurses, patients, and pharmacists. In 1999, Lilly gave an "[REDACTED]" to a company called Pragmaton in Chicago, Illinois to develop a "[REDACTED]" series on "[REDACTED]". The project developed into a live presentation by Dr. Sumer Verma. The participants earned professional credits for "[REDACTED]". Specifically, the presentation provided one credit to physicians toward the AMA Physician's Recognition Award; one ACPE credit for pharmacists; and one continuing education credit for nurses. For this presentation, Dr. Verma received a "[REDACTED]" from Lilly, "[REDACTED]" from Lilly, and endorsement from Lilly's Speakers Bureau. ([REDACTED])

134. One of the goals of Dr. Verma's presentation was to enable participants to "[REDACTED]". In the presentation, Dr. Verma noted that elderly patients were good candidates for anti-psychotics

because they "[REDACTED]." However, she did not mention that TD was a known side effect of Zyprexa, as Lilly was later required by the FDA to disclose in its labeling. Instead, Dr. Venna simply recommended the prescription of anti-psychotics to treat elderly people who act "[REDACTED]." ([REDACTED])

135. In an undated Eli Lilly outline entitled "F[REDACTED]
[REDACTED]", Lilly outlines several key areas with regard to expanding the use of Zyprexa among primary care physicians. In the outline, Lilly acknowledges that the FDA's limited Zyprexa indications and label safety concerns may be possible barriers to new uses. Lilly then goes on to question, "[REDACTED]
[REDACTED]" ([REDACTED])

136. In an October 2000 document produced from the files of Lilly's James Delisle, entitled, "[REDACTED]", Lilly states that "[REDACTED]" is to "[REDACTED]
[REDACTED]
[REDACTED]" "[REDACTED]" is the patient who is "[REDACTED]" and "[REDACTED]" is the elderly "[REDACTED]" patient. ([REDACTED]
[REDACTED])

137. Lilly then goes on to "[REDACTED]" — "[REDACTED]
[REDACTED]." Here, "[REDACTED]" is "[REDACTED]" and "[REDACTED]" is "[REDACTED]." Lilly continues by explaining that additional target symptoms will be "[REDACTED]" and honoraria and primary care preceptorships are included as budget items to implement the strategies. At no time has Zyprexa been approved for agitation, anxiousness, or treatment-resistant depression. Lilly wrongly used market research and not scientific and medical research to uncover "[REDACTED]"

██████████" to suggest additional patient markets and promotional themes. (██████████
██████████)

138. In a letter dated August 20, 1999, Acting Director, Dr. Russell Katz, of the Division of Neuropharmacological Drug Products of the U.S. Department of Health and Human Services, told Lilly that its study of olanzapine in patients with bipolar disorder should not include patients with depression. The Acting Director explained that "██████████
██████████
██████████
██████████" (██████████
██████████)

139. In a Clinical Investigator's Brochure concerning the 1996 study F1D-MC-H6AO, Lilly submitted a May 2000 summary that states: "██████████
██████████
██████████
██████████
██████████
██████████
██████████
██████████" (██████████)

140. Despite studies and data that confirm the lack of efficacy and significant health and safety risks associated with the off-label promotion of Zyprexa for the elderly, Lilly continues to profit from this practice.

3. **Fraudulent and Unlawful Acts Regarding Off-Label Promotions for Pediatric Usage**

141. In order to gain additional sales and to compete with other antipsychotics such as Risperdal, Lilly undertook a scheme to market and promote Zyprexa for off-label purposes, including for use in the treatment of children suffering from disorders such as depression, anxiety, Attention Deficit Disorder (ADD), Attention Deficit Hyperactivity Disorder (ADHD), and sleep disorders and to generally promote Zyprexa's use in children as a mood stabilizer. Zyprexa is not now and never has been approved by the FDA for any use in children, not even for use in children with schizophrenia and bipolar disorder.

142. Use of Zyprexa for children and adolescents is commonplace. One investigative report concerning the use of antipsychotic medication in treatment centers for troubled children in Westchester, Rockland and Putnam counties in the State of New York, indicated that between 60% and 90% were on some sort of psychotropic drugs. At the St. Agatha Home in Nanuet, New York it has been reported that about 85 of the 100 children are treated with psychotropic drugs. The home's psychiatrist conceded that pharmaceutical representatives visit him about three times a week. The reporter noted that, "[REDACTED]".

143. An undated Lilly communication marked "[REDACTED]" underscores the Lilly's efforts to promote Zyprexa use in children despite the lack of FDA approval. "[REDACTED]"

_____” The communication specifically instructs sales personnel:

██████████” However, it goes on to provide the sales representatives with a verbatim answer if they

[REDACTED]

([REDACTED]) Despite the lack of any clinical trials or FDA approval for the use of Zyprexa in children, Lilly specifically addressed the promotion of pediatricians and trained its sales force on how pediatricians could obtain and prescribe Zyprexa to their young patients.

144. While emphasizing Zyprexa's "[REDACTED]" Lilly felt it important to include dosages for even of label use. They pointed out that 2.5 mg is a "[REDACTED]" for "[REDACTED]" as well as for the treatment of Tourettes Syndrome and stuttering, two more off-label uses. ([REDACTED]). Lilly's own doctor, Dr. Bruce Kinon, recommended a 2.5 mg starting dose for children because 5mg/day could be "[REDACTED]" "[REDACTED]." However, in the same e-mail, Dr. Kinon suggested that some adolescents could be treated with up to 20mg/day. ([REDACTED]).

145. Lilly clearly anticipated eventual approval of Zyprexa for children and adolescents and for indications that far exceeded schizophrenia and bipolar mania. Lilly sponsored several studies in the 1990s to determine the effects of olanzapine on children and adolescents for a variety of symptoms. One study sought to "[REDACTED]"
[REDACTED]
[REDACTED]"
([REDACTED]) Another studied the effect of olanzapine on patients aged 6-16 for "[REDACTED]" ([REDACTED]) One study's objective stated

“ [REDACTED] ”
[REDACTED] ”
([REDACTED]) Long before Zyprexa was approved for anything related to bipolar disorder in any population, another study proposed “ [REDACTED] ”
[REDACTED] ”
([REDACTED]) A similarly designed trial studied the effect of olanzapine on bipolar disorder on patients as young as 5 years old. ([REDACTED]) (In that study, 2 of 23 patients discontinued due to adverse events and 3 patients reported spontaneous adverse events.)
([REDACTED])

146. On September 21, 1998, the European Agency for the Evaluation of Medical Products contacted Lilly affiliates regarding the periodic safety update reports it submitted during late 1997 and early 1998. The EAEMP informed Lilly affiliates that “ [REDACTED] ”
[REDACTED]
[REDACTED]
[REDACTED] ” ([REDACTED]). In an undated document produced from the files of Julie A. Birt of Lilly, “ [REDACTED] ”, Lilly details the pediatric use of Zyprexa for conditions that included child onset schizophrenia, bipolar disorder, pervasive development disorder, autism, mental retardation, Tourettes and anorexia nervosa. ([REDACTED])

147. Zyprexa has never been proven safe or effective for the off-label uses promoted by Defendant and the intermediary marketing firms. As a result children were and continue to be exposed to medication which, at best, is ineffective and, at worst, can and does cause life-threatening illnesses such as diabetes and diabetes-related complications.

148. Children and adolescents remain a powerful market for Lilly's Zyprexa. Pediatric sales of Zyprexa totaled approximately \$500 million between 1999 and 2005. On November 1, 2005 Leila Abboud of The Wall Street Journal reported that "[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]."

[REDACTED]

[REDACTED]

[REDACTED]" Not only does Lilly continue to promote the use of Zyprexa in children for non-approved indications, it is well aware of the success and profitability of this off-label promotion.

4. **Fraudulent and Unlawful Acts Regarding Off-Label Promotions for “Donna” and Other Depressed Patients**

149. Lilly's global long-term marketing plan is perhaps best summed up by the slogan it adopted in 1995: "[REDACTED]." This first slogan aptly characterizes Lilly's strategy for Zyprexa from its inception – to make Zyprexa part of the everyday prescribing habits of not only psychiatrists but primary care physicians as well. ([REDACTED])

150. Lilly encouraged PCPs to prescribe Zyprexa "off-label" for various "[REDACTED]" patient complaints. Lilly instructed PCPs that "[REDACTED]" and that "[REDACTED]" "[REDACTED]." Lilly's marketing materials encourage the PCPs to use the "p[REDACTED]" "[REDACTED]" to treat for "[REDACTED]", "[REDACTED]", "[REDACTED]", "[REDACTED]", "[REDACTED]", "[REDACTED]" and "[REDACTED]." The materials also tout that Zyprexa "[REDACTED]" so that once a patient is put on this powerful antipsychotic, they can be maintained on it. To convince PCPs of the efficacy and safety of Zyprexa for such routine use, Lilly relied upon psychiatrists and primary care physicians who were paid as consultants to

provide "[REDACTED]" for its aggressive marketing program. ([REDACTED])

151. In a lengthy overhead training presentation from 1998, Lilly went into great detail about the need to expand the use of its "[REDACTED]" products in the PCP market in order to maximize profits and remain competitive because of the "significant" role PCPs play in most markets and the fact that "[REDACTED]"

" ([REDACTED]) As an example, Lilly looked at "[REDACTED]"

" which included "[REDACTED]"

" and imagining "[REDACTED]"

" ([REDACTED])

152. Lilly also created several promotional characters or typical patient sketches to market Zyprexa to PCPs. Lilly's marketing materials describe, among others, "[REDACTED]" as a mother of two children in her early 30s who is "[REDACTED]", has "[REDACTED]" and cannot "[REDACTED]". Donna has been on SSRIs for depression in the past but has never been prescribed an anti-psychotic. Lilly encourages her PCP to prescribe Zyprexa for Donna even though she has not been diagnosed with either bipolar mania or schizophrenia. ([REDACTED]).

153. In preparation for its PCP Marketing Launch in September 2000, Lilly distributed a "[REDACTED]" which served as a "[REDACTED]" for sales representatives attempting to implement Lilly's PCP message. Lilly states, "[REDACTED]"

[REDACTED]". To guide its sales representatives, Lilly created fictional characters such as "[REDACTED]". Lilly directed its sales representatives to persuade PCPs not to refer patients to psychiatrists because, "[REDACTED]". At the same time, Lilly directed sales representatives to push Zyprexa's "[REDACTED]" by telling PCPs that there is no need for blood monitoring when using Zyprexa and that there are no black box warnings on the product. In a section of the guide referred to as "[REDACTED]", Lilly educates its sales representatives on how to underplay evidence on weight gain and treatment emergent diabetes if the PCP were to raise the issue. ([REDACTED])

154. Lilly pushed Zyprexa for broad-based treatment of symptoms rather than diagnoses. In internal email correspondence in February 2000, Lilly's Ajay K. Bhardwaj reflected on a presentation on US market research that he attended:

[REDACTED]

(b) (7)(C), (b) (7)(D) This statement was forwarded to key players at Lilly by Roland Powell of Lilly with a note that it was particularly “(b) (7)(C), (b) (7)(D)”. (b) (7)(C), (b) (7)(D)

5. Ongoing Refusal to Disclose Known Adverse Effects

155. Less than seven weeks after Zyprexa's approval, Lilly faced charges that it was suppressing side effects. The FDA sent to Lilly a letter on November 14, 1996 outlining labeling pieces and promotional activities considered to be "[REDACTED]" by the Division of Drug Marketing, Advertising, and Communications (DDMAC). ([REDACTED])

156. According to the agency, the promotional campaign lacked "[REDACTED]
[REDACTED]" in that they "[REDACTED]
[REDACTED]" In
addition, the materials did not "[REDACTED]
[REDACTED]" including weight gain. In
conclusion, the letter stated that the labeling pieces "[REDACTED]
[REDACTED]
[REDACTED]" ([REDACTED])

157. The FDA's letter specifically referenced an interactive teleconference conducted by Dr. Gary Tollefson, Vice President of Lilly Research Laboratories, on October 2, 1996 – two days after FDA approval. The letter states:

[REDACTED]

([REDACTED]) The information on weight gain was indeed included in the approved labeling, but as an adverse event, not a therapeutic benefit. Since the product was approved at the time of this teleconference, Dr. Tollefson knew or should have known what information the approved labeling contained and in what section it appeared. His statements were therefore, false and misleading. Further, Dr. Tollefson's misrepresentations about weight gain on the phone conference were belied by Lilly's own study's conclusion. Tollefson claimed that the weight gain was mostly observed in patients whose weights were abnormally low before taking Zyprexa, hence the alleged therapeutic effect. However, Lilly's own study in 1993 concluded that "[REDACTED]

[REDACTED]." ([REDACTED]) Dr. Tollefson's interactive telephone conference is an eerie and early compilation of the lies, misrepresentations, data manipulations concerning the risks and benefits of Zyprexa that Lilly has continued to report for more than a decade.

158. Moreover, the FDA complained that the October 1, 1996 teleconference had "[REDACTED]" [REDACTED] " Dr. Tollefson had said that olanzapine had no Parkinsons-like side effects: "[REDACTED]

[REDACTED]
[REDACTED]

" And: " [REDACTED]
[REDACTED]
[REDACTED] " Years later, however, Lilly admitted on its " [REDACTED]
[REDACTED] " for Zyprexa that it could " [REDACTED]
[REDACTED] ".

159. In the October 1, 1996 conference call, Dr. Tollefson announced that prolactin would not be a problem: " [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED] "

160. While Dr. Tollefson hawked Zyprexa as an anti-psychotic that did not require blood monitoring, Lilly's own officials doubted it. In the margin of the copy of the Tollefson transcript that was produced from the files of Kelly B. Freeman, a Lilly official hand-wrote next to Dr Tollefson's statement that blood monitoring is " [REDACTED]
[REDACTED] ". Lilly believed, as early as 1996 that blood glucose monitoring was recommended for patients on Zyprexa. Nevertheless, they allowed their spokesman, Dr. Tollefson, to distinguish Zyprexa from its competitors as a treatment option that did not require monitoring, leaving the impression that Zyprexa was less expensive to prescribe than other anti-psychotics because it did not require blood monitoring.

161. Dr. Tollefson continued: "[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] " By contrast, however, Lilly later said that patients should commence with 2.5 to 5 mg on day one. ([REDACTED]) From the very first days of Zyprexa, and with full knowledge of Lilly's highest executives, scientists and medical officers, Lilly was pushing the envelope with Zyprexa. From day one, Lilly made misleading statements about Zyprexa.

162. Dr. Tollefson was not alone in misleading physicians about Zyprexa. In an October 1, 1996 press release titled "[REDACTED]" issued by Lilly press spokesperson, Lori Roberts, Lilly said that Zyprexa had "[REDACTED]" "[REDACTED]," quoting Dr. Gary Tollefson, VP of Lilly's Research Laboratories and "[REDACTED]." Further, the press release promised that "[REDACTED]" ([REDACTED]).

a. Fraudulent and Unlawful Acts Regarding the Suppression of the Risk of Weight Gain

163. Weight gain is an acknowledged side effect of both first and second generation antipsychotic medications. Nearly fifty years of research have linked antipsychotics to weight

gain as a side effect. For example, chlorpromazine and similar conventional antipsychotics have been known to impair glucose metabolism, which can lead to weight gain, following its introduction in the 1940s. Nevertheless, Lilly went to great lengths to conceal this potentially sales-crushing side effect until, at last, confrontation of the weight gain issue became unavoidable.

164. Prior to the launch in 1996, Lilly knew or should have known that Zyprexa causes weight gain. In a Lilly-sponsored study conducted from October 1993 to November 1993 it was found that "[REDACTED]" – just four weeks. This study was titled "[REDACTED]" and dated November 30, 1993. Conclusions from later analysis were summarized in "[REDACTED]" in April 1995. ([REDACTED])

165. In May 1998, Lilly conducted a European Planners Meeting in Barcelona, Spain on the subject of "[REDACTED]". At that meeting, Lilly informed participants to "[REDACTED]" and emphasized the "[REDACTED]". Lilly stressed that weight gain should not be discussed unless a physician raised the subject, in which case it should be dealt with as a class side effect. ([REDACTED])

166. Later in 1998, Lilly debated whether it should disclose the risk of weight gain to physicians and patients. After the publication of articles linking Zyprexa with hyperglycemia, Peter Clark proposed in an email dated November 30, 1998 that Lilly add the following statement to its labels: "[REDACTED]". Mr. Clark's suggestion

was rejected and Lilly decided to continue to ignore the issue of weight gain. ([REDACTED]
[REDACTED])

167. At a February 16, 2000 Franchise Team Meeting a Weight Change slide show was given and also distributed to the Zyprexa team electronically. It included a Global Market Research Summary slide; "d [REDACTED]

_____” It continued with “_____”

 _____.” A list of Lilly Marketing initiatives and
 Medical Research studies to address weight gain followed. (_____)

168. Lilly ultimately acknowledged that during a three year study "[REDACTED] [REDACTED]." However, it attempted to minimize this result by characterizing it as a "class effect" and by claiming that "[REDACTED] [REDACTED]." In fact, Lilly's own graphs included with the three year study show that approximately 75% of patients gained weight and that approximately 50% gained over 11 pounds. ([REDACTED]). Only when Lilly was in danger of losing all credibility on the weight gain issue did Lilly finally own up to the problem. The sales force is now being trained to minimize the importance of weight gain to physicians admitting that up to 56% of patients realized significant weight gain. This document provides a "[REDACTED]" for discussion of the weight gain issue. ([REDACTED])

b. Fraudulent and Unlawful Acts Regarding the Suppression of the Risk of Hyperglycemia and Diabetes

169. While Zyprexa sales continued to escalate exponentially each year, Lilly

continued to hide the adverse effects its drug was having on the elderly, children, those diagnosed with schizophrenia and others.

170. Even before the case reports in the peer-reviewed medical literature became known to the general medical public, Lilly was aware of large numbers of diabetes-related adverse events associated with Zyprexa, as reflected in the adverse event reports ("AERs") on file with the FDA's Medwatch database. The numbers of AERs over the first four years of Zyprexa's market life, showing nearly 200 AERs after 2 years, 400 AERs after 3 years, and nearly 600 diabetes-related AERs in Zyprexa's fourth year of distribution were reported to the FDA and known to Lilly.

171. These numbers are very conservative. It is well understood that for prescriptions drugs, adverse drug event reports only represent between 1% and 10% of the total estimated population of all complications. (See Physician Knowledge, Attitude and Behavior Related to Reporting, Archives of Internal Medicine, 1988: 148; 1589-1592; Underreporting of Hemorrhagic Stroke Associated with Phenylpropanolamine, 286(24) JAMA (2001); Rhode Island Physician's Recognition and Reporting of Adverse Drug Reactions, RI Medical Journal 1987: 70:311-316.). The reality of under-reporting is due mainly to the fact that the adverse event reporting system in the U.S. is a voluntary system (i.e. doctors are under no obligation to report an adverse event). As a result, the number of reported complications must be multiplied by a factor of between 10 and 100 in order to arrive at the true estimated number of complications. After adding the unreported complications to the above figures, the true number of diabetes-related adverse events from market introduction in 1996 to year end 2000, is estimated to be as low as 6,000 and as high as 60,000, a staggeringly high number considering the indications being treated and the availability of far safer alternatives.

172. As of September 1998, there were approximately 150 diabetes related AERs, but not a single reference was made to these significant adverse event reports in the label. Indeed, the first time any reference is made in Zyprexa's U.S. label to any post-market adverse event of any type is on September 30, 1998. Even then, buried in a portion of the label entitled "[REDACTED]" and in inconspicuous print, Lilly only warned that "priapism" (prolonged erection) had been an adverse event reported since market introduction that was "[REDACTED]".

173. Between September 30, 1998 and March 17, 2000, Lilly made three more label changes. Again, after a total of 400 diabetes-related AERs, Lilly still did not add any diabetes-related adverse event to its label, including the post-market adverse event section, but continued to mention, buried deep within the label, that the only adverse event reported was "priapism".

174. On April 12, 2000, Lilly finally included a reference to "diabetic coma" together with priapism as an adverse event that had been reported since Zyprexa's market introduction. In light of the date of this label change, however, this change did not make its way into the 2000 PDR, but is first found in the 2001 PDR. Further, this reference is again buried deep within the label, as inconspicuously as possible, and fails to reference the hundreds of other diabetes-related injuries, namely, diabetic deaths, ketoacidosis not resulting in coma as well as countless cases of diabetes and hyperglycemia.

175. Thus, the sole mention of any diabetes-related conditions in Zyprexa's label from October 1996 to April 12, 2000 was in a list at the end of the product label entitled, "[REDACTED]" that included "[REDACTED]" such conditions as "[REDACTED]", "[REDACTED]", and an "[REDACTED]" number of pre-market diabetes and hyperglycemia adverse events and a "[REDACTED]" number of pre-market cases of diabetic

acidosis. Lilly knew by 1996 that Zyprexa's link to diabetes was scientifically well established in the medical literature and in its own clinical trials and that it warranted an adequate warning to the medical community. Even after being confronted by an alarming number of post-marketing AERs, Lilly did nothing to warn the medical community of the true dangers linked to Zyprexa.

176. Lilly simply ignored the reports of adverse events concerning diabetes, elevated glucose levels, and diabetes. In notes taken of a December 14, 1998 ACNP luncheon meeting with Jack Gorman, the writer noted that Jack "[REDACTED]" [REDACTED]. Lilly, in fact, had already implemented this marketing strategy, blaming diabetes and hyperglycemia on the schizophrenic population at large, rather than on Zyprexa. Yet, Mr. Gorman did think that patients with over 10% baseline weight "[REDACTED]" [REDACTED]. Lilly, however, continued to resist this advice despite mounting Adverse Event Reports. A requirement for blood glucose monitoring could narrow the gap between Zyprexa and its competitors and negatively impact sales. ([REDACTED])

177. In an internal Lilly email dated February 16, 1999 to Dr. Bruce Kinon of Lilly, Bruce Basson writes that there was a "[REDACTED]" in glucose and cholesterol levels among olanzapine patients over three years. He calls it a "[REDACTED]"

178. On August 17, 2000, Eli Lilly's "[REDACTED]"
 "[REDACTED]" met to discuss how Lilly should go about dealing with mounting concerns about
 Zyprexa use, weight gain, and diabetes. David Allison, Ph.D. noted that "[REDACTED]"
 "[REDACTED]" and
 that "[REDACTED]"
 "[REDACTED]"

179. Dr. Breier's and Lilly's position that no proof exists that there is a direct link between Zyprexa and diabetes was the subject of much early debate among Lilly doctors and executives including Charles M. Beasley, Paul Berg, Patricia Cavazzoni, Alan Breier and Robert Baker. On October 9, 2000, Dr. Thomas Brodie wrote to Robert Baker on behalf of a group of endocrinologists hired as consultants for Lilly who had met the weekend before with Drs. Breier, Baker and others. He began:

[REDACTED]

([REDACTED])

180. That same day, Dr. Robert Baker responded to Dr. Brodie's e-mail, noting

[REDACTED]

([REDACTED]) Dr. Baker's seemingly reversed concern that hyperglycemia threatens olanzapine is accurate and indicative of Lilly's true worry – that Zyprexa sales could be affected by widespread knowledge that the drug causes an increased risk of hyperglycemia and diabetes.

181. Dr. Beasley responded to Drs. Breier, Baker, and Berg with his take on the concerns of Lilly's consulting endocrinologists:

[REDACTED]

([REDACTED])

182. Dr. Baker's response to Dr. Beasley's e-mail is both chilling and an accurate description of Lilly's marketing cum medical position concerning diabetes. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]." ([REDACTED])

183. Just days after the above e-mail exchange, Lilly issued its approved "[REDACTED]" dated October 16, 2000. In it, Lilly noted that Zyprexa was implicated in a "[REDACTED]" of case reports that related alterations in glucose metabolism with antipsychotics. Addressing this concern, Lilly responded that a large data analysis performed by Lilly "[REDACTED]"

[REDACTED]

[REDACTED]." In other words, Zyprexa was no more likely than a placebo to alter glucose metabolism. The document also stated that [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED].” ([REDACTED])

184. Lilly followed up the Standby Statement on December 29, 2000 with the issuance of “[REDACTED]” to be used by Zyprexa sales representatives in responding to questions about, inter alia, weight gain and increased risk of diabetes. This 30 page manual describes the biological aspects of diabetes and related weight gain and instructs sales representatives on how to assure prescribing physicians that there no reason to believe that use of Zyprexa presents an increased risk for diabetes. ([REDACTED])

185. Not everyone at Lilly was certain that weight gained while on Zyprexa was unrelated to health problems such as diabetes and cardiovascular risks. On March 21, 2001, and just five months after issuing the Standby Statement, Dr. Beasley stated in an e-mail that

[REDACTED]

([REDACTED])

6. Texas Medication Algorithm Project (TMAP) Activities

186. Lilly devised another method of increasing its Zyprexa sales: infiltrating and corrupting the ordinary processes of state government in Texas, Pennsylvania, and elsewhere in order to encourage utilization of Zyprexa. Lilly entered into an association-in-fact with certain

Texas, Pennsylvania, and other state government employees in which they all agreed to affirmatively push the use of Zyprexa and other SGAs for both on- and off-label purposes in return for ongoing payments to state authorities.

187. The market for antipsychotics is largest in state Medicaid agencies because of the overwhelming number of people with severe mental illnesses insured by those programs. Lilly, along with other pharmaceutical companies, recognized that getting Medicaid agencies to endorse and promote the use of expensive atypical antipsychotics would be a boon for the company's bottom line. Further, in addition to increasing state utilization of Zyprexa and other atypical antipsychotics, Lilly knew Medicaid acceptance of the use of Zyprexa would influence the private network of insurance to pay for the drug as well, thereby bringing sales to an even higher level.

188. In 1995, an alliance of individuals from the pharmaceutical industry, the University of Texas, and the mental health and corrections systems of Texas created the Texas Medication Algorithm Project (TMAP), a project funded in part by money from pharmaceutical companies in general and Lilly in particular. TMAP was designed to foster overwhelming use of expensive atypical antipsychotics by producing a set of guidelines and a formulary of specific drugs approved as first and second line treatment for schizophrenia, bipolar disorder, and depression. The guidelines mandate use of the most expensive antipsychotics on the market – specifically Zyprexa and its competitors – by physicians working with the Texas Medicaid agency. On April 1, 1998, Zyprexa was approved “[REDACTED]” by TMAP. Lilly has used this approval to convince PCPs that Zyprexa is safe to prescribe for “[REDACTED]” symptoms.

189. The choice of Zyprexa as a first-line option for treatment is not accidental. Lilly

provided kickbacks to Texas state officials involved with TMAP to the tune of at least \$175,000 between 1997 and 2004. Records show at least twenty-one separate payments from Lilly to TMAP officials during that period, some of which were deposited directly into the personal accounts of TMAP officials.

190. Once TMAP reached the conclusion it was designed to reach – promoting utilization of atypical antipsychotics for first-line treatment for both on-label and certain off-label indications – Lilly and other pharmaceutical manufacturers provided major funding for the exportation of TMAP to other states. They sponsored TMAP staff, through unrestricted educational grants, as they presented 71 seminars for groups of clinical providers, professional groups, administrators, payers, Medicaid officials, and other stakeholders in an effort to spark interest in implementing TMAP in other states. As a result of the seminars, several states expressed interest in implementing the algorithm project in their own mental health systems, causing the Texas Department of Mental Health and Mental Retardation to note that “[REDACTED]

191. In April 2002, senior federal officials established the New Freedom Commission on Mental Health to conduct a “[REDACTED]” “[REDACTED].” The commission issued recommendations in 2003, including a commendation of TMAP as a “[REDACTED]” medication treatment plan that “[REDACTED]” “[REDACTED].” Twenty-five federal agencies, including the Substance Abuse and Mental Health Services Administration (SAMHSA), were instructed to develop a nationwide implementation plan based on those recommendations.

192. TMAP and the national effort have come under fire recently. Allen Jones of the Pennsylvania Office of the Inspector General revealed that “[REDACTED]

[REDACTED]

[REDACTED].” He noted that the “[REDACTED]” that developed TMAP was actually behind the New Freedom Commission recommendations for a nationwide program and were “[REDACTED]

[REDACTED]

[REDACTED].” Clearly, the goals of TMAP and the proposed nationwide expansion of the program did not include ensuring the best treatment for the mentally ill but instead were focused solely on increasing pharmaceutical company profits and ensuring ongoing payments to state authorities.

7. National Alliance for the Mentally Ill (NAMI) Activities

193. Lilly also utilized a non-profit organization as a front to further its own purposes of increasing market share for atypical antipsychotics and other medications. Lilly’s funding and partnering with the National Alliance for the Mentally Ill (NAMI) in the late 1990s and early 2000s was designed to accomplish through a non-profit organization what it could not on its own: giving the appearance of independent analysis and a grassroots movement encouraging the use of atypical antipsychotics by state and private insurers. The scheme worked and Lilly certainly benefited from its significant donations to NAMI. Zyprexa was the leading antipsychotic in the world in 2000, capturing nearly 40% of the global antipsychotic market. A year later, Zyprexa was the sixth highest selling pharmaceutical product in the world, with \$3.2 billion in sales.

194. NAMI is a national association of mental health organizations in every state and bills itself as “[REDACTED]

[REDACTED].” In reality, this not-for-profit organization readily accepts donations offered by pharmaceutical manufacturers while

[REDACTED]

[REDACTED]

[REDACTED].”

195. Lilly has been the largest contributor among pharmaceutical manufacturers to NAMI, giving the organization approximately \$2.87 million between 1996 and 1999.

196. Lilly “donations” to NAMI were not limited to money. In 1999, Mother Jones Magazine reported that Lilly executive Jerry Radke was “on loan” to NAMI as an executive. Also in 1999, Bob Postlethwait, a Lilly executive who headed the group that produced and marketed Zyprexa (and Prozac), assisted NAMI Indiana in securing government funding for an executive director.

197. Lilly also provided funding for a variety of brochures and programs produced by NAMI highlighting the use of atypical antipsychotics. One such Lilly-funded brochure – “Understanding Schizophrenia” – produced by NAMI for patients and families of schizophrenics minimizes the side effects of atypical antipsychotics such as Zyprexa. Another – the 2001 “Access to Effective Medications” brochure produced by NAMI National for legislators and paid for by Lilly – lays out a blueprint for nationwide NAMI lobbying of state governments to reduce or remove any limitations to payments for atypical antipsychotics, again down-playing the side effects of such drugs.

198. Using money from Lilly and other pharmaceutical companies, NAMI – both the various state-level associations and the national organization – has effectively lobbied state and federal governments to increase spending on atypical antipsychotic drugs and to reduce restrictions on access to those pharmaceuticals, thereby protecting pharmaceutical industry profits through the guise of independent, grassroots advocacy. For example, between 1998 and

2000, Lilly gave NAMI Washington State \$91,000. During that time, NAMI Washington State, in an effort led by NAMI lobbyist Brad Boswell, lobbied the state legislature for \$1 million specifically for atypical antipsychotic drugs. Brad Boswell was Lilly's Washington state lobbyist just prior to his assignment with NAMI Washington State. NAMI also joined a suit initiated by the Pharmaceutical Research and Manufacturers of America (PhRMA) against the state of Michigan in order to increase physician access to higher cost pharmaceuticals – including atypical antipsychotics – under the state's Medicaid program.

199. The U.S. Department of Health and Human Services Office of the Inspector General issued a report in 2002 warning that cozy financial relationships between non-profit advocacy groups and pharmaceutical companies -- such as the one between NAMI and Lilly -- which result in the generation of revenue for the pharmaceutical companies could be considered illegal under the federal anti-kickback statute.

8. "Success" of the Unlawful Marketing Enterprises

200. The unlawful marketing activities during the years 1996 through 2000 were wildly successful, with Zyprexa moving from no market share to the most market share in antipsychotic prescriptions.

201. Lilly's early marketing efforts were to position itself as the newest SGA and better than Risperdal. The marketing plan did not distinguish between on-label and off-label purposes, and the plan was successful. Even in the first quarter of sales, Zyprexa was prescribed for numerous off-label purposes, aiding to the overall success of Lilly's Zyprexa launch.

202. Over the next four years -- 1997, 1998, 1999, and 2000 -- Lilly's ongoing unlawful marketing plan facilitated Zyprexa's meteoric rise. Each year Zyprexa sales increased at double digit rates. The number of off-label prescriptions grew each year. Zyprexa became the number one prescribed antipsychotic for schizophrenia. By 2000, Zyprexa's United States sales totaled

approximately \$1.94 billion.

II. 2000: Label Change and FDA Warning

1. FDA Rebuffed Lilly's Attempts to Imply Olanzapine Had Been Approved to Treat Adolescents

203. Lilly sought to increase sales by obtaining FDA approval to treat adolescents with Zyprexa tablets, NDA 20-592. As Dr. Russell Katz of the FDA wrote to Lilly in a letter dated April 6, 2000, the first step was to get the FDA's approval to run a trial study on adolescents:

You have been advised that the Pediatric Final Rule (63 FR 66632) requires that all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that your Proposed Pediatric Study Request was submitted to NDA 20-592 (Zyprexa tablets) on February 25, 2000 and received February 28, 2000. A formal Written Request will be forwarded to you under separate cover.

(Letter from Russell Katz to Gregory Brophy (Apr. 6, 2000)) The FDA reminded Lilly that adolescent treatment was not approved until Lilly first ran "an assessment of the safety and effectiveness." In this slap of the hand, the FDA told Lilly that it would have to meet the FDA's "formal" requirements.

204. In an undated letter that may have been written around November 9, 2000, Dr. Russell Katz of the FDA wrote to Dr. Brophy of Lilly. Dr. Katz basically warned that Zyprexa had not yet been approved for pediatric use and that they did not yet know whether there was "a health benefit" for adolescents:

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632) (21 CFR 314.55 (or 601.27)). FDA is deferring submission of the pediatric assessments of safety and effectiveness

that may be required under these regulations until we have had an opportunity to more carefully consider the question of whether or not there may be a health benefit from studies in pediatric patients, and if so, in which populations. FDA will inform you on or before June 1, 2001, whether pediatric studies are required under the rule. If FDA determines at that time that pediatric studies are necessary, FDA will also set a specific time at which you must submit the required assessments.

(Letter from Russell Katz to Gregory Brophy (undated), available at www.accessdata.fda.gov)

205. Lilly had been pushing Zyprexa for adolescent use. The FDA reminded Lilly that any such use would be a “new indication[]” that would require formal review. Lilly had not previously submitted “an assessment of the safety and effectiveness of the product in pediatric patients.”

2. In 2000, the FDA Approved a New Indication for the Maintenance of Treatment of Schizophrenia, But Rejected Lilly’s Attempt to Broaden the Indication to “Psychotic Disorders”

206. Prior to October 2000, Lilly “propose[d] the use of Zyprexa (olanzapine) tablets for the maintenance of treatment response.” (Letter from Russell Katz to Gregory Brophy (Oct. 12, 2000)) The FDA only agreed to approve this new indication on the condition that Lilly adopt the FDA’s “revisions to the 3 sections of labeling” which required Lilly to specify Zyprexa’s narrow indication for schizophrenia. *Id.*

207. It is impossible to ascertain the full extent of the label revisions mandated by the FDA because twenty-three pages of Dr. Katz’s October 12, 2000 “action letter” approving this new indication were redacted from the publicly available copy. However, the unredacted material in Dr. Katz’s letter illustrates that Lilly tried to broaden the new indication through expansive language in the label.

208. The FDA required Lilly to specify Zyprexa’s narrow indication for schizophrenia. It also required Lilly to insert “treatment of schizophrenia” in lieu of “management of the

manifestations of psychotic disorders” in the “CLINICAL PHARMACOLOGY, Clinical Efficacy Data-Schizophrenia” section. Further, the FDA required Lilly to replace “in psychosis” with “in schizophrenia” in the same section. The FDA had Lilly replace “management of the manifestations of psychotic disorders” with the narrower “treatment of schizophrenia” in the “INDICATIONS AND USAGE, Schizophrenia” section. And the FDA required Lilly to replace “Antipsychotic efficacy” with the narrower “Efficacy in schizophrenia” in the “DOSAGE AND ADMINISTRATION, Schizophrenia—Usual Dose” section.

209. These examples demonstrate that Lilly was trying to expand the use of Zyprexa by changing the label to infer that Zyprexa was appropriate for the broader treatment of “psychosis” rather than for the narrower indication of schizophrenia. The FDA rebuffed this attempt to move outside the approved indication. However, Lilly was not to be deterred. Having been denied approval for expansion of the indications for Zyprexa use in the label, Lilly continued to use its network of enterprises for off-label promotion of those indications.

3. **In February 2000, the FDA Approved a New Indication to Treat Bipolar Mania and Lilly Rejoiced that There Were No New Safety Issue on Dementia in the Label**

210. On February 24, 2000, Lilly’s Vice President of Pharmaceutical Products, Alan Breier, announced in an internal email that the FDA had approved olanzapine for treatment of bipolar mania. ([REDACTED]) It was “[REDACTED]” and olanzapine was “[REDACTED] [REDACTED].” *Id.* Yet, Mr. Breier mostly enthused over Lilly’s ability to keep serious new risks off the label:

[REDACTED]

[REDACTED]

([REDACTED]) Lilly hid the risks and massaged the label to minimize safety concerns.

But they were legally and ethically obliged to do just the opposite.

4. In February 2000, European Regulators Asked for a Full Review of Prior Adverse Event Reports

211. Although Lilly had been in possession of adverse event data and internal studies demonstrating the risk of diabetes associated with Zyprexa for years, not until regulatory agencies in Europe and the United States pressured Lilly to provide clinical data, review prior studies, and assess the safety of olanzapine did Lilly do so. Lilly begrudgingly obeyed, but only under compulsion.

212. On February 21, 2000, the European Agency for the Evaluation of Medicinal Products ("EAEMP") sent a telefax to Mr. J.C. Saunder of Eli Lilly Ltd. UK. Specifically, Dr. Juhana Idanpaan-Heikkila of the EAEMP ordered Lilly to step up its review of risk factors and provide that information to the EAEMP: "[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] " ([REDACTED])

213. Further, the EAEMP requested full review of all known cases of diabetic ketoacidosis: "[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] "

([REDACTED]) Lilly was aware of numerous instances of diabetic ketoacidosis. In an NDA Periodic Report, Lilly had previously reported three incidents of ketoacidosis from April 1 to June 30, 1998. ([REDACTED]) In another Periodic Adverse Drug Event Report, Lilly had previously reported five instances of diabetic acidosis and two instances of diabetic coma between September 30 and December 30, 1997. ([REDACTED]) Lilly had failed to clearly disclose those instances to the European regulatory authorities.

214. Rather than provide critical information as it arrived, Lilly waited for regulatory authorities in both Europe and the United States to demand a thorough accounting of the risks of olanzapine.

5. In May 2000, the FDA Asked Lilly to Look at Larger Patient Pools and Conduct a Thorough Assessment of Previous Studies But Lilly Spun the Science According to Its Marketing Strategy

215. The FDA evidently did not trust the research done by Lilly on diabetes and hyperglycemia, in part, because of the small numbers of patients treated in each study.

Consequently, on May 1, 2000, the FDA sent Lilly “ [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED].” ([REDACTED]

[REDACTED]) The FDA basically told Lilly that it needed credible data on diabetes and hyperglycemia.

216. Specifically, the FDA asked for the following information, apparently not trusting that Lilly had previously and fully disclosed these harms:

[REDACTED]

[REDACTED]

([REDACTED]) In addition, the FDA had required a "[REDACTED]
[REDACTED]
[REDACTED]." *Id.* The FDA also wanted "[REDACTED]
[REDACTED]." *Id.*

217. Nearly three months later, Lilly partially responded to the FDA's request of May 1, 2000. Gregory T. Brophy, Director of Lilly's US Regulatory Affairs, sent a letter to the FDA on July 31, 2000. Dr. Brophy attached a "Note to Reviewer" to his letter. The Note to Reviewer stated: "[REDACTED]
[REDACTED]
[REDACTED]." ([REDACTED])

218. As part of its July 31, 2000 response to the FDA, Lilly submitted an analysis of 78 controlled trials. In addition, Lilly provided "[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]." ([REDACTED])
[REDACTED]) However, most of the information was misleading, especially as it pertained to full disclosure of the risks of prolactin, weight gain, and hyperglycemia.

219. Lilly misled the FDA on prolactin. In "[REDACTED]" of the "[REDACTED]
[REDACTED]", Lilly suggested that Zyprexa did not elevate prolactin levels, writing [REDACTED]

[REDACTED]
[REDACTED]
[REDACTED]” ([REDACTED]
[REDACTED]) Lilly implied that olanzapine did not produce heightened prolactin levels. But Lilly’s own proposed label of October 2000 admitted the risk of heightened prolactin: “[REDACTED]
[REDACTED]
[REDACTED]” In July 2000, however, Lilly said that risperidone was “[REDACTED]”

220. Lilly also misled the FDA on weight gain. In “[REDACTED]” of the “[REDACTED]” submitted on July 31, 2000, Lilly admitted that [REDACTED]
[REDACTED]
[REDACTED]” Sticking to formula, Lilly deflected responsibility from its own drug and dispersed blame among the class as a whole. Lilly spent nearly an entire page discussing study after study on—of all things—clozapine’s association with weight gain. In a subsequent short paragraph, Lilly mentioned that “[REDACTED]
[REDACTED]” and “[REDACTED]
[REDACTED]” These bare references to olanzapine masked the fact that olanzapine was among the top one or two atypical antipsychotics for weight gain. Lilly’s discussion of clozapine only clouded the picture.

221. In “[REDACTED]” of its July 31, 2000 attachment, Lilly told the FDA that “[REDACTED]
[REDACTED]” ([REDACTED]) But Lilly downplayed the

results:

[REDACTED]

Lilly absurdly suggested that all patients enrolled in studies gain weight and, therefore, it was not olanzapine's fault if those patients gained weight too. Lilly did not mention that its own 1993 study had shown "[REDACTED]" and consistent weight gain among olanzapine patients. ([REDACTED]) Nor did Lilly mention the possibility that olanzapine caused weight gain. Instead, Lilly practiced its blame-the-victim marketing strategy on the FDA.

222. Lilly tried to hide the likelihood of hyperglycemia, blaming it on pre-disposed factors among schizophrenic patients. In the "[REDACTED]" attached to its July 31, 2000 letter, Lilly told the FDA:

[REDACTED]

223. Lilly effectively blamed the victims. To Lilly, it was the pre-disposed factors that made hyperglycemia more likely – not olanzapine. What this explanation intentionally overlooked was that increased incidence of diabetes in Zyprexa users appeared in studies in which *all* subjects were diagnosed schizophrenics. Since Zyprexa increased the incidence of diabetes over placebo when both the Zyprexa group and the placebo group were schizophrenics, Lilly's assertion that schizophrenics are pre-disposed to diabetes did nothing to exonerate Zyprexa. Lilly was aware of this fact but continued to push the pre-disposition explanation rather than admit to the dangers associated with its blockbuster drug.

224. In "[REDACTED]," Lilly claimed that hyperglycemia simply occurred in the population at large and that olanzapine produced no risk of hyperglycemia:

[REDACTED]

([REDACTED]) Lilly claimed that olanzapine led to no more hyperglycemia than a placebo, and it said that 78 trials supported this conclusion. In actuality, Lilly knew that hyperglycemia occurred more often under olanzapine than in placebo.

225. Almost one year later, on May 21, 2001, Lilly sent a second letter to the FDA to complete its response to the original FDA letter of May 1, 2000 requesting further information on the risks of diabetes and hyperglycemia. ([REDACTED]) Gregory T. Brophy, the director of Lilly's U.S. Regulatory Affairs, sent the FDA a "[REDACTED]" [REDACTED]. He attached a "[REDACTED]" (" [REDACTED] ") to his letter. ([REDACTED])

226. The Note summarized Lilly's additional research. Lilly had analyzed data from an "[REDACTED]" database with thousands of patients on antipsychotics. Lilly concluded from this database that hazard ratios for diabetes were 3.5 for conventional antipsychotics, 3.1 for atypical antipsychotics, and 3.0 for olanzapine. In addition, Lilly analyzed a British database called the "[REDACTED]" with 8 million patients from the United Kingdom. Lilly found that [REDACTED] [REDACTED]. The hazard ratio for atypical antipsychotics was 3.3.

227. On top of analyzing these larger pools, Lilly summarized its own clinical trials. That showed "[REDACTED]". In essence, this was an admission that patients on olanzapine had higher levels of glucose. Lilly finally concluded that "[REDACTED]".

"[REDACTED]" This was another admission. But, as usual, Lilly deflected responsibility by pointing its finger at competitors and older antipsychotics with similar problems.

228. Lilly's response to the FDA's inquiries was of a piece with its overall strategy for dealing with concerns that Zyprexa was associated with diabetes. Whether responding to the FDA or prescribing doctors, Lilly consistently employed the two dodges of pre-disposition and class effect to deflect inquiries about what its own studies had demonstrated that Zyprexa increases the incidence of diabetes in patients who take it. An internal Lilly memorandum confirms this fact, stating "[REDACTED]".

6. In October 2000, the FDA Required Lilly to Add the Risks of Diabetic Coma and Neuroleptic Malignant Syndrome to the Label and to Delete Language That Suggested Olanzapine Did Not Increase Glucose Levels

229. On May 9, 2000, Lilly submitted a "[REDACTED]" to the FDA. ([REDACTED])

[REDACTED], reporting that "[REDACTED]".

[REDACTED]") Lilly claimed that this label change was based on [REDACTED].

"[REDACTED]" ([REDACTED]) According to Lilly, this label

change was not connected to the FDA's letter of May 1, 2000 because Lilly had received that letter one day *after* proposing the May 9, 2000 label change.

230. Specifically, Lilly sought two changes to the Zyprexa label in its proposal of May 9, 2000:

[REDACTED]

[REDACTED]

[REDACTED]

Id. On July 31 2000, Gregory Brophy, Director of US Regulatory Affairs at Lilly, repeated this same offer to change the label in a letter to the FDA. ([REDACTED])

231. The phrase "diabetic coma" was inserted into the label after the FDA approved it via a letter to Lilly dated October 11, 2000. However, the FDA rejected Lilly's proposed "[REDACTED] [REDACTED]." As a result, there were no changes in the ADVERSE REACTIONS, Additional Findings Observed in Clinical Trials, Laboratory Changes section from 1996 until at least January 2004. That section remained precisely the same from 1996 through 2003.

232. The reason why the FDA rejected Lilly's proposed change to that section in 2000 was because Lilly's proposed revision was misleading. In essence, Lilly tried to say that olanzapine caused no increase in glucose levels. This is the text that Lilly proposed:

[REDACTED]

[REDACTED]

This summary suggested that random glucose levels were the same in olanzapine patients as a placebo. If Lilly had its way, this misleading statement would have been inserted into the ADVERSE REACTIONS, Additional Findings Observed in Clinical Trials, Laboratory Changes section. But the FDA said, "no."

233. On October 11, 2000, Dr. Russell Katz, Director of the Division of Neuropharmacological Drug Products, Office of Drug Evaluation I, FDA Center for Drug Evaluation and Research, wrote to Gregory T. Brophy, Director of US Regulatory Affairs, regarding the October 2000 proposed label change. Dr. Katz felt that the paragraph on glucose levels would be misleading:

[REDACTED]

The FDA characterized Lilly's proposed statement as "[REDACTED]" for the label. To Dr. Katz and the FDA, Olanzapine was not as safe as Lilly made it out to be. There was simply not enough data and analysis to support Lilly's proposed revision to the label. And the FDA would not permit Lilly to use the label as a marketing device to infer "[REDACTED]"

that was not proven to exist.

234. As a result of the FDA's refusal in 2000, the ADVERSE REACTIONS, Additional Findings Observed in Clinical Trials, Laboratory Changes section was not revised until years later when the FDA approved language that told the truth--i.e., olanzapine increased the level of glucose. The olanzapine label that was ultimately revised on September 20, 2005 warned:

[REDACTED]

This is what the FDA was looking for all along. But Lilly did not provide it in October 2000 when it denied that olanzapine led to glucose increases.

235. In his letter of October 11, 2000, Dr. Russell Katz of the FDA approved a new warning for Neuroleptic Malignant Syndrome (NMS). Dr. Katz said the following addition to the "[REDACTED]" section was "[REDACTED]," pending Lilly's submission of 20 paper copies of the "[REDACTED]";

[REDACTED]

In other words, from October 2000 onwards, Lilly would have to warn about NMS on the label. This was a first.

236. Dr. Katz approved the addition of "[REDACTED]" to the label warnings in his letter dated October 11, 2000. This addition to the "[REDACTED]" section was "[REDACTED]" pending submission of "[REDACTED]." Lilly was obligated to insert the term "[REDACTED]" into the "[REDACTED]" subsection of the "ADVERSE

REACTIONS" section. As a result, the label subsequently warned:

Adverse events reported since market introduction which were temporally (but not necessarily causally) related to ZYPREXA therapy include the following: allergic reaction (e.g., anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, pancreatitis, and priapism.

(Zyprexa Zydis Label (revised 2003) ("action date" of Jan. 14, 2004)) The term "diabetic coma" had not previously appeared in this section until the FDA's requirement of October 11, 2000.

I. 2001-2002: Ongoing Operations of the Unlawful Marketing Enterprises

237. Despite the mounting evidence known to Lilly regarding the adverse weight gain, hyperglycemia, diabetes, cardiovascular, and other risks of Zyprexa, the lack of superior comparative efficacy of Zyprexa to other antipsychotics and the recklessness of their off-label promotions, in the early 2000's Lilly continued its ongoing operation of the Zyprexa Unlawful Marketing Enterprises and planned to further market Zyprexa for use in patients for whom the drug's approval was never intended. According to an internal document, Lilly decided that "[REDACTED]

[REDACTED]
[REDACTED]" These new indications included "[REDACTED]
[REDACTED]" ([REDACTED])

238. In order to reach those goals, Lilly undertook a massive strategy change in late 2000 and began to target primary care physicians with the aim of increasing their utilization of Zyprexa. ([REDACTED]) The strategy encouraged physicians to focus on symptoms and behaviors rather than diagnoses, emphasizing how Zyprexa is "[REDACTED]
[REDACTED]" ([REDACTED])
Suppression of side effects and metabolic risks continued to be part and parcel of the plan.

I. Continued and Growing Knowledge of Adverse Side Effects

239. As Lilly continued to downplay the risks of Zyprexa to consumers, doctors, and the FDA, more and more of its own studies and clinical trials conclusively demonstrated the life-threatening risks associated with the use of its drug.

240. In a study entitled "[REDACTED]" with an amended protocol dated March 9, 2001, Lilly noted "[REDACTED]" and that "[REDACTED]" ([REDACTED])

241. While most of the attention to date had been on the glucose and metabolic side effects of Zyprexa, they were not the only risks of which Lilly was aware. In March 2001, Ernie Anand of Lilly brought to the attention of some of his colleagues an article on atypical antipsychotic cardiovascular risk. He noted that it was "[REDACTED]" and that the "[REDACTED]" In response, Dr. Charles Beasley stated that "[REDACTED]" In the same breath, however, Dr. Beasley pointed out:

[REDACTED]

[REDACTED]

([REDACTED])

242. An April 6, 2001 Lilly internal analysis of its UK General Practice Research database (GPRD) found that patients treated with either conventional or atypical antipsychotics had a higher risk of developing diabetes during exposure to the drug. The risk was found to be higher for those taking atypicals such as olanzapine and risperidone than for those taking conventional antipsychotics. As the study states, "[REDACTED]

[REDACTED]."

[REDACTED] ([REDACTED]) The study also notes that

[REDACTED]

([REDACTED]) This study was forwarded for discussion in an e-mail sent by John Holcombe on April 9, 2001, where he calls it "the most recent version of the epidemiological data from the GPRD regarding antipsychotic drug use and dia[REDACTED]." ([REDACTED] 219615 [REDACTED] (6)

243. The companion study entitled "[REDACTED]" analyzed a prescription claim database and concluded [REDACTED]

[REDACTED]." ([REDACTED]) The study abstract, dated

April 18, 2001, also noted [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]” ([REDACTED]) Further, the authors stated, [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]” ([REDACTED])

[REDACTED]

244. On April 12, 2002, Lilly conducted a Policy Committee Meeting on the Zyprexa safety overview, addressing clinical data on weight gain and diabetes in connection with Zyprexa use. In summarizing the clinical data on diabetes, Lilly draws attention to a “[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]” Continuing on metabolic issues, Lilly states that “[REDACTED]

[REDACTED]” and that “[REDACTED]

[REDACTED]” Instead of working to protect

patients from these effects, Lilly focused on continuing sales, concluding “[REDACTED]

[REDACTED]

[REDACTED]” ([REDACTED]

[REDACTED])

2. Suppression of Side Effects and Risks

245. In early 2001, Lilly was well aware that Zyprexa was among the worst of the antipsychotics in terms of weight gain. In a “[REDACTED]” slide set presentation dated February 2001, Lilly stated that the main “[REDACTED]” of olanzapine, as compared to its competitors, were weight gain, sedation, value for money, and reduction of depressive episodes.

In fact, Zyprexa ranked at the very bottom of its competition on weight gain and ability to avoid sedation. (████████████████████)

246. Despite this knowledge, Lilly attempted to avoid or minimize the issue, misleading physicians as to the degree, manageability, and incidence of weight gain in olanzapine patients. Further, Lilly adopted a campaign summed up by the words "[REDACTED]" instructing its sales force to tell psychiatrists and physicians that "[REDACTED] [REDACTED]
[REDACTED]."

()

247. In a February 8, 2001 presentation for the "[REDACTED]," Lilly instructed sales representatives on how to address mounting concerns among prescribing physicians about Zyprexa use and weight gain, hyperglycemia, and diabetes. Market research indicated "[REDACTED]"

§ 87(2)(b)

Accordingly, Lilly directed the force to "[REDACTED]"
[REDACTED]
[REDACTED] " [REDACTED]
[REDACTED] ([REDACTED]) Sales
representatives were thus instructed to "[REDACTED]" with them to handle the
objections of the two types of physicians. ([REDACTED])

248. The "[REDACTED]" [REDACTED]

[illegible]

249. Overall, the strategy appeared to work for Lilly. Initial market research showed a

14. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] ([REDACTED]

[REDACTED])

250. In March 2001, Lilly further revised its “

██████████e" to help its sales force when "██████████
██████████." (██████████) The strategy guide notes "██████████

██████████." (██████████) Despite the stated differences in
blood glucose for patients on Zyprexa and the known connection between increased blood
glucose and diabetes, Lilly continued to tell physicians that "██████████

██████████." (██████████)

251. Concurrently, Lilly developed other materials "██████████

██████████" based on the
company's belief that "██████████

██████████." (██████████) These materials, including slide
sets, studies, physician management tools, and trainings, were designed to "██████████

██████████," provide data to "██████████" for use in
presentations on Zyprexa and weight gain or hyperglycemia/diabetes, and provide "██████████

██████████." (██████████
██████████)

252. In a June 20, 2001 "██████████

██████████." (██████████

██████████.) Part of McKinsey's

recommended strategy entailed Lilly acknowledging weight gain, diabetes, and hyperglycemia as "[REDACTED]" rather than avoiding the issue. However, a second part involved a new "[REDACTED]" aimed at emphasizing Zyprexa's efficacy "[REDACTED]" while showing diabetes risk was a class effect rather than one limited to olanzapine. This strategy was to be used in the United States, Canada, France, and the UK. ([REDACTED]) Lilly followed the second part to the letter, but continued to omit a warning about the "[REDACTED]" of diabetes and hyperglycemia for years to come.

253. Lilly instead continued to sidestep questions about the risk of treatment-emergent diabetes while on olanzapine. In two marketing presentations from 2001, Lilly informed its sales force "[REDACTED]"

[REDACTED]
[REDACTED]" Regarding diabetes, Lilly states

[REDACTED]

1) [REDACTED]

2) [REDACTED]

3) [REDACTED]

4) [REDACTED]

5) [REDACTED]

([REDACTED]) Not addressing the "[REDACTED]"

"[REDACTED]" unless raised by a physician is both a violation of the mandate of fair and balanced information and a willful omission of material fact, especially given Lilly knew that many PCPs were not aware of the issue.

254. Concurrently, and in line with its avoidance of the "[REDACTED]," Lilly continued to emphasize that treatment with Zyprexa was "[REDACTED]" and "[REDACTED]" promoting the claim in marketing brochures in October 2001. ([REDACTED])

255. In April 2002, the Japanese government forced Lilly to revise its label in Japan and warn of the risk of treatment-emergent diabetes. Even after the Japanese government mandated that Lilly include warnings of the risk of diabetes (after only nine adverse event reports), Lilly continued to omit any warning of diabetes from its Zyprexa label in the United States.

256. Notably, Lilly knew long before April 2002 that the Japanese government had serious concerns about Zyprexa's safety. In an email dated September 25, 2001 (only about 3 months after Zyprexa was launched in Japan), Takashi Taniguchi, a representative of Eli Lilly's Japanese affiliate, directed an email to Lilly's Timothy F. Parshall and several other Lilly insiders concerning "[REDACTED]". Due to its' significance, Mr. Parshall subsequently forwarded the email to Lilly's Jared G. Kerr. In the email, Mr. Taniguchi stated:

[REDACTED]

[REDACTED]

[REDACTED]?

[REDACTED]

[REDACTED]?

[REDACTED]
[REDACTED]
[REDACTED]”
[REDACTED])

257. Despite this substantial evidence linking Zyprexa use with diabetes and/or hyperglycemia, Lilly continued to down-play these problems. In mid-2002, a Lilly market research analyst wrote:

[REDACTED]

[REDACTED])

258. Lilly's suppression or manipulation of side effects and risks of olanzapine did not go unnoticed. On June 15, 2002, Eli Lilly's Dennis G. West sent an email to Dr. John Newcomer, a one-time Lilly consultant, concerning a mailing Lilly sent to physicians focusing on positive statements about Zyprexa made by John Buse, M.D, another consultant for Lilly. The email also related to previous discussions between Mr. West and Dr. Newcomer relating to Zyprexa use and its relationship to glucose/insulin irregularities. Mr. West stated:

[REDACTED]

([REDACTED]) Lilly did not make a change in their warnings to this effect until September of '03.

259. Dr. Newcomer immediately took exception to Mr. West's comments and accused Lilly of engaging in a "[REDACTED]." Specifically, Dr. Newcomer stated,

[REDACTED]

[REDACTED]

[REDACTED]

([REDACTED])

260. The sales force raised a similar concern shortly thereafter. In internal email correspondence dated September 13, 2002 with the subject line "[REDACTED]" sales representative Jerry D. Clewell asked

[REDACTED]

[REDACTED]

([REDACTED]) Despite Dr. Newcomer's concern that Lilly was playing fast and loose with study results and the connection between olanzapine use and diabetes and questions from the sales force about such connections, Lilly stuck to the party line. Robert Browne, Senior Outcomes Research Advisor for Lilly, responded that he had not heard of any such plans to send "[REDACTED]" to physicians. ([REDACTED])

3. Off-Label Promotion to Primary Care Physicians

261. Lilly began promoting Zyprexa to primary care physicians in September 2000.

([REDACTED]) The strategy, building on the 1996-2000 off-label campaign to target various forms of depression, sought to position Zyprexa as a "[REDACTED]" and "[REDACTED]" "[REDACTED]" References to this positioning abound in Lilly's internal documents, testifying to the strength of the effort directed at the PCP market.

262. In an undated overhead training presentation entitled "[REDACTED]", Lilly identified the "[REDACTED]" for opening the door to the elderly market for Zyprexa: "[REDACTED]" ([REDACTED]) Lilly instructed the sales force that patient profiles "[REDACTED]" and that the focus should be on "[REDACTED]" such as "[REDACTED]" rather than